National Institute on Drug Abuse
Advancing Addiction Science

Publications
Revised February 2019

Teaching Addiction Science

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Teaching Addiction Science

Originally developed to help scientists and teachers in discussions with high school students and others about how drugs of abuse act in the brain. The original slides have been replaced with Powerpoint presentations. These presentations cover the basic functions of the brain, the neurobiological basis for addiction, and the actions of heroin and cocaine, ecstasy and others.

The Brain & the Actions of Cocaine, Opioids, and Marijuana

The first in a 5-part series, offers an understanding of the brain, how the reward center works, and what happens in the brain when a person uses cocaine, opioids (heroin), or marijuana.

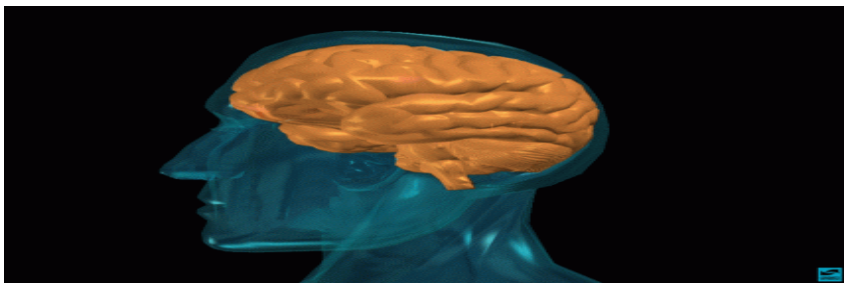
The objective of the presentation is to inform students (high school) how 3 drugs of abuse (cocaine, opiates, marijuana) actually work in the brain. The presentation is arranged in 3 sections. The first section introduces the brain and presents some basic neurobiology, the second introduces the reward pathway and the third presents the mechanism of action of each drug and how each affects the reward system.

This presentation can be downloaded as a Powerpoint file - The Brain & the Actions of Cocaine, Opioids, and Marijuana (PPT, 4.1MB) and was last reviewed in November, 2019

Expand All

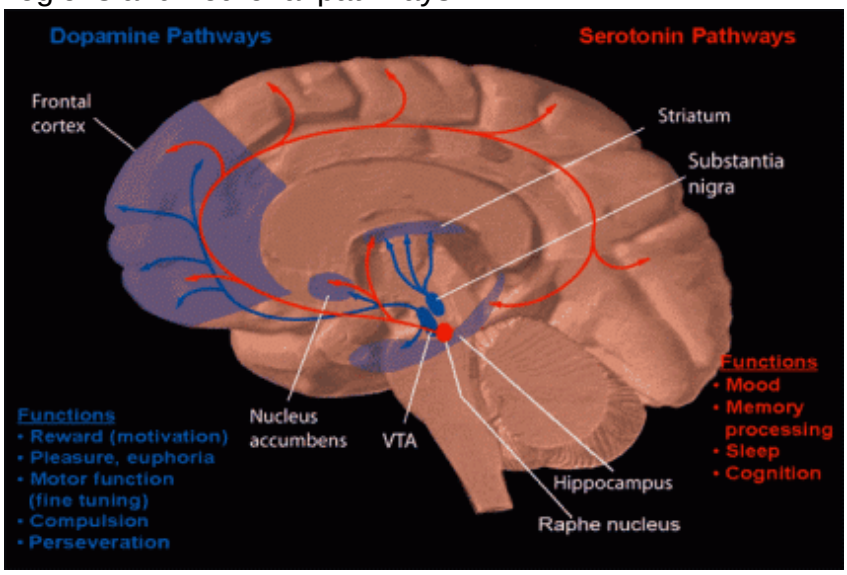
Introduction to the Brain

Introduction



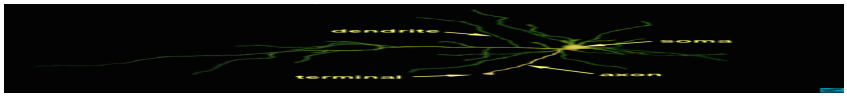
Introduce the topic of your talk. Indicate that you will explain how the brain basically works and how drugs such as cocaine, opioids and marijuana interact with the brain's normal activities. Tell students that you will introduce the concept of "reward" which is the property that is characteristic of many addictive drugs. Describe the brain as a functional unit; it is made up of billions of nerve cells (neurons) that communicate with each other using electrical and chemical signals.

Brain regions and neuronal pathways



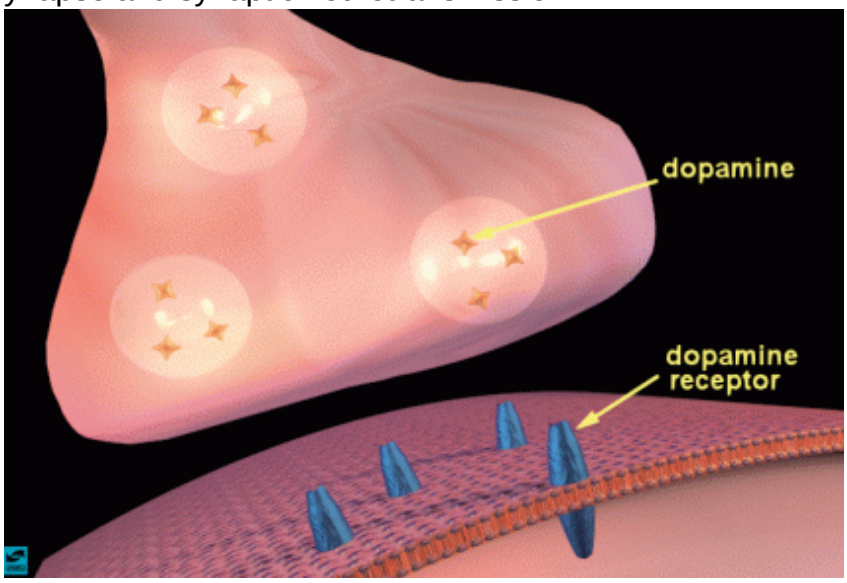
Certain parts of the brain govern specific functions. Point to sensory, motor, association and visual cortex to highlight specific functions. Point to the hippocampus to highlight the region that is critical for memory, for example. Indicate that nerve cells or neurons travel from one area to another via pathways to send and integrate information. Show, for example, the reward pathway. Start at the ventral tegmental area (VTA) (in blue), follow the neuronal path to the nucleus accumbens (purple), and then on to the frontal cortex. Explain that this pathway gets activated when a person receives positive reinforcement for certain behaviors ("reward"). Indicate that you will explain how this happens when a person takes an addictive drug.

Neuronal structure



Remind the student that pathways are made up of neurons. Describe the anatomy of a neuron (soma, dendrites, and axon are marked with text). State that this neuron is real - as viewed through a microscope. Explain the normal direction of impulse flow. Dendrites and soma receive chemical information from neighboring neuronal axons. The chemical information is converted to electrical currents which travel toward and converge on the soma. A major impulse is produced (the action potential) and travels down the axon toward the terminal. Point to the terminal.

The synapse and synaptic neurotransmission

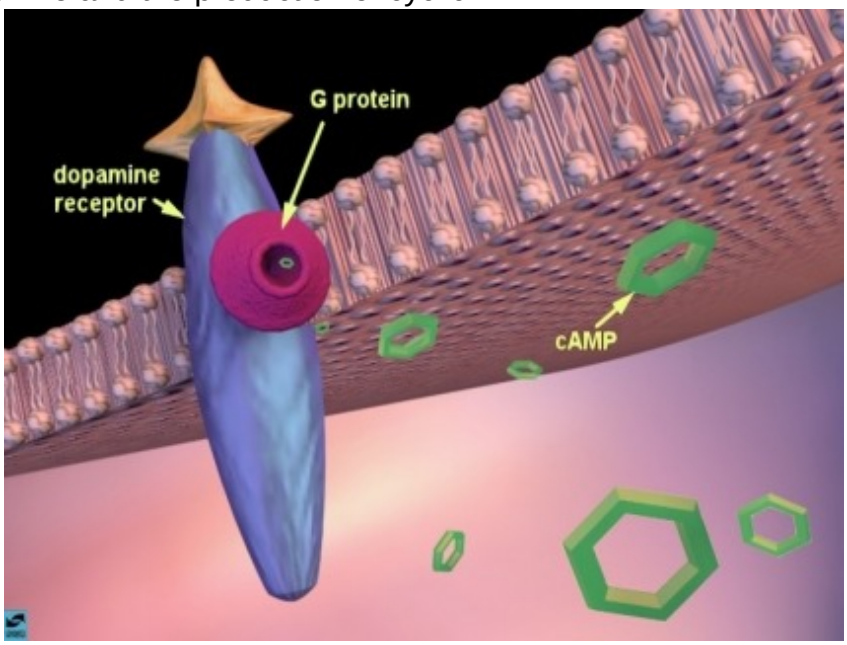


Describe the synapse and the process of chemical neurotransmission. Indicate how vesicles containing a neurotransmitter, such as dopamine (the stars), move toward the presynaptic membrane as an electrical impulse arrives at the terminal. Describe the process of dopamine release (show how the vesicles fuse with the presynaptic membrane). Once inside the synaptic cleft, the dopamine can bind to specific proteins called dopamine receptors (in blue) on the membrane of a neighboring neuron. Introduce the idea that occupation of receptors by neurotransmitters causes various actions in the cell; activation or inhibition of enzymes, entry or exit of certain ions. State that you will describe how this happens in a few moments.

Dopamine neurotransmission

Using the close-up of a synapse, continue using dopamine for your example of synaptic function. Explain that it is synthesized in the nerve terminal and packaged in vesicles. Reiterate the steps in neurotransmission. Show how the vesicle fuses with the membrane and releases dopamine. The dopamine molecules can then bind to a dopamine receptor (in blue). After the dopamine binds, it comes off the receptor and is removed from the synaptic cleft by uptake pumps (also proteins) (in red) that reside on the terminal. This process is important so that not too much dopamine is left in the synaptic cleft at any one time. Also point out that there is a neighboring neuron, which releases another compound called a neuromodulator. In this case it is an "endorphin" (blue flying saucers). Endorphins bind to opioid receptors (in green) which reside on the post-synaptic cell or in some cases on the terminals of other neurons (this is not shown so it must be pointed out). The endorphins are destroyed by enzymes rather than removed by uptake pumps.

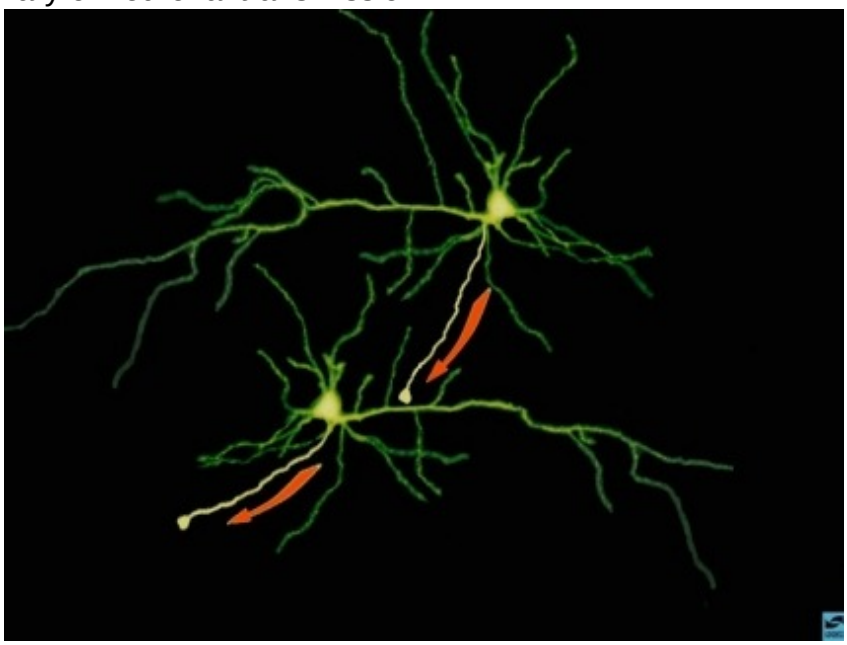
Dopamine and the production of cyclic AMP



Using the close-up view, explain what happens when dopamine binds to its receptor. When dopamine binds to its receptor, another protein called a G-protein (in pink) moves up close to the dopamine receptor. The G-protein signals an enzyme to produce cyclic adenosine monophosphate (cAMP) molecules (in green) inside the cell. [Sometimes the signal can

decrease production of cAMP, depending on the kind of dopamine receptor and G-protein present.] Point to the dopamine receptor-G-protein/adenylate cyclase complex, and show how cAMP is generated when dopamine binds to its receptor. Indicate that cAMP (point to the cyclic-looking structures) controls many important functions in the cell including the ability of the cell to generate electrical impulses.

Summary of neuronal transmission



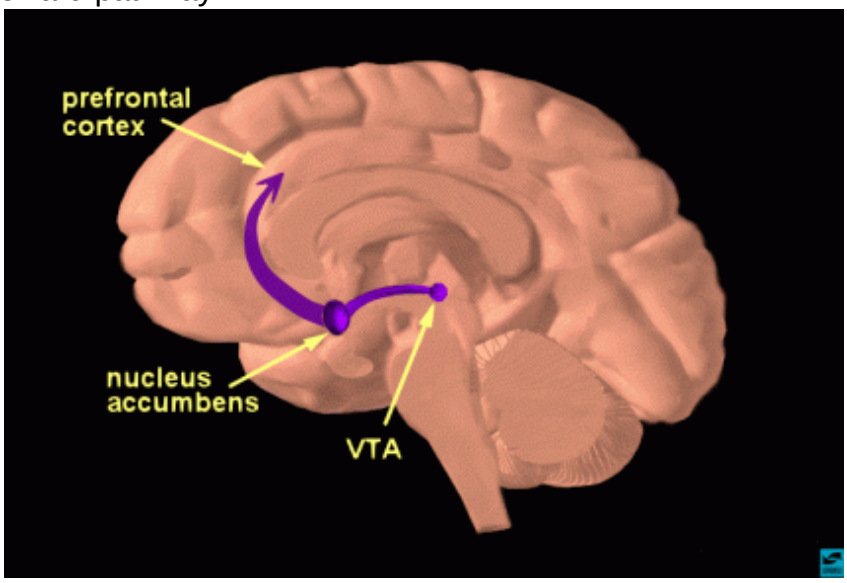
Use the example of two neurons making contact to summarize neuronal transmission. Point to the cell on the top and indicate that electrical impulses flow in the direction toward the terminal. Remind the students what happens when impulses reach the terminal; neurotransmitters are released, they bind to their receptors, and new impulses are generated in the cell on the bottom. Explain that this is how information travels from neuron to neuron.

Introduction to the Reward System

Reward: drug self-administration

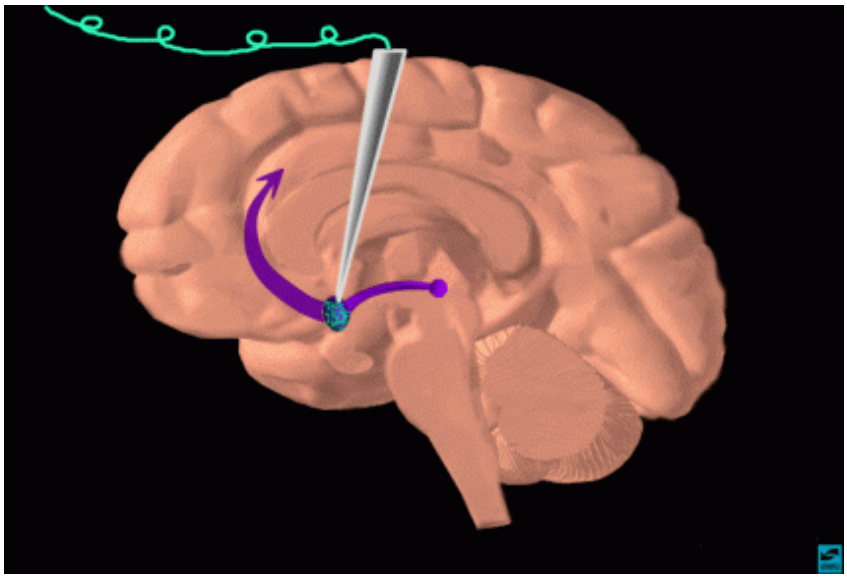
Introduce the concept of positive reinforcement or reward. Explain that rats will press a lever to self-administer an injection of cocaine or heroin that is inserted into either the peripheral bloodstream (left image) or into specific brain regions (right image). The rat keeps pressing to get more cocaine or heroin because the drugs make the rat feel so good. This is called positive reinforcement, or reward. Natural rewards include food, water, and sex - each is required to maintain survival of our species. Animals and people will continue to exhibit a behavior that is rewarding, and they will cease that behavior when the reward is no longer present. Explain that there is actually a part of the brain that is activated by natural rewards and by artificial rewards such as addictive drugs. This part of the brain is called the reward system. Neuroscientists have been able to pinpoint the exact parts of the brain involved, with the help of the rats. Point to the cartoon on the right and explain that rats will also self-administer addictive drugs directly into their brains, but only into a specific area of the reward system. If the injection needle is moved less than a millimeter away from this crucial area, the rat won't press the lever for more drug. So based on information from working with the rats, scientists have drawn a map of the brain, and located the structures and pathways that are activated when an addictive drug is taken voluntarily. Tell the students that you will show them this "map."

The reward pathway



Tell students that this is a view of the brain cut down the middle. An important part of the reward system is shown and the major structures are highlighted: the ventral tegmental area (VTA), the nucleus accumbens (nuc. acc.) and the prefrontal cortex. Also, the pathway connecting these structures is highlighted. The information travels from the VTA to the nucleus accumbens and then up to the prefrontal cortex. Reiterate that this pathway is activated by a rewarding stimulus. [Note to scientists - this is not the only pathway activated by reward, other structures are involved too, but only this part of the pathway is shown for simplicity.]

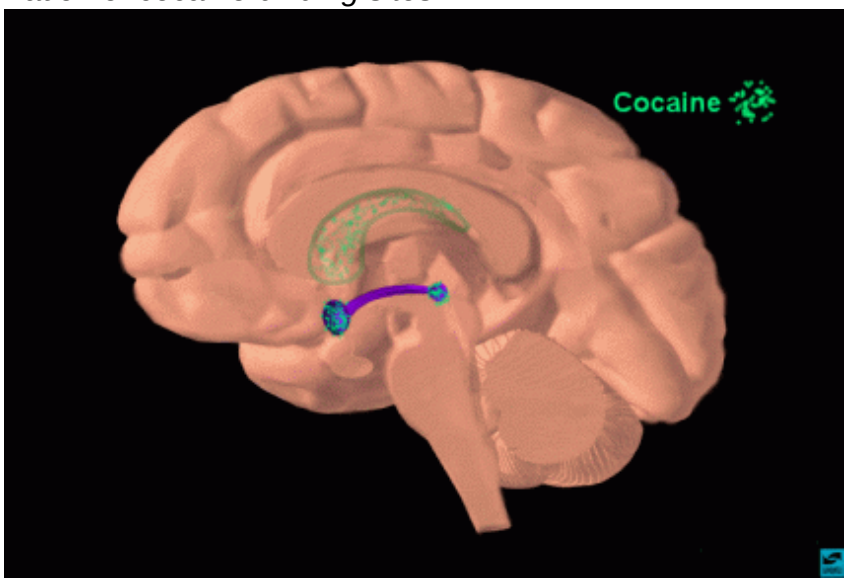
Injection of cocaine into the nucleus accumbens



Demonstrate how scientists located the structures important for the addictive nature of drugs. Show that a rat will self-administer cocaine directly into the nucleus accumbens (or the VTA) to activate the pathway. Point to an area close to the nucleus accumbens or VTA and state that if the injection is placed in this other area, the rat will not press the lever to receive the drug. Indicate that scientists know a lot more than where the drug acts to produce rewarding effects - they also know how the drugs work. Show examples with cocaine, heroin, and marijuana.

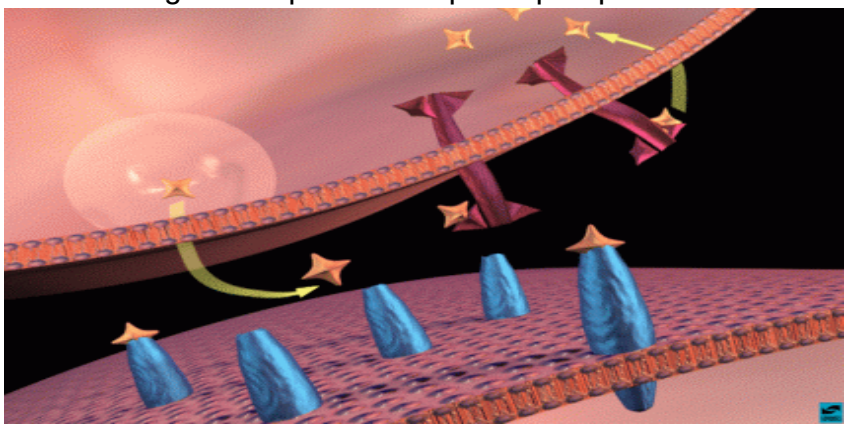
Introduction to Drugs of Abuse: Cocaine, Opiates (Heroin) and Marijuana (THC)

Localization of cocaine *binding sites*



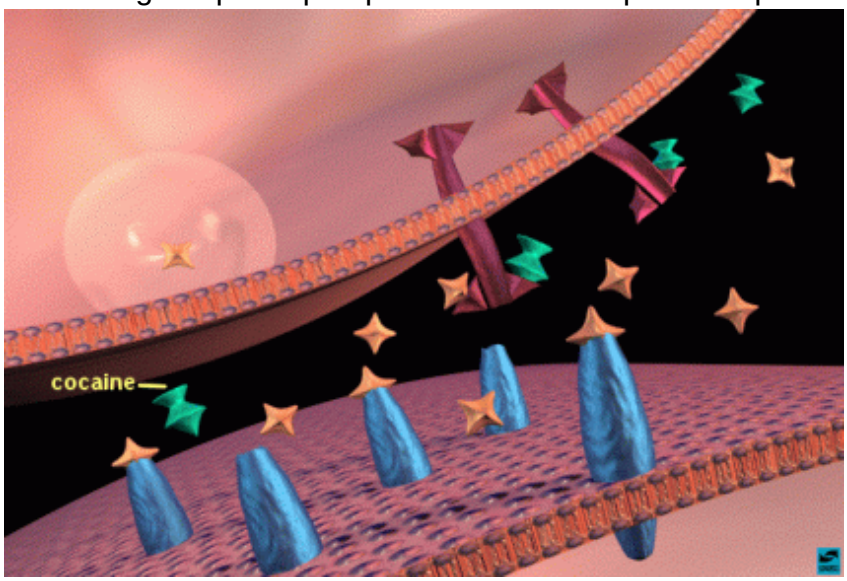
When a person smokes or snorts cocaine, it travels quickly to the brain. Although it reaches all areas of the brain, it concentrates in some specific areas. These are highlighted with the turquoise sprinkles; the VTA, the nucleus accumbens, and the caudate nucleus (lighter turquoise since the caudate is inside the hemisphere). Point out that cocaine concentrates especially in the reward areas that you have just discussed. Cocaine accumulation in other areas such as the caudate nucleus can explain other effects such as increased stereotypic behaviors (pacing, nail-biting, scratching, etc..)

Dopamine binding to receptors and uptake pumps in the nucleus accumbens



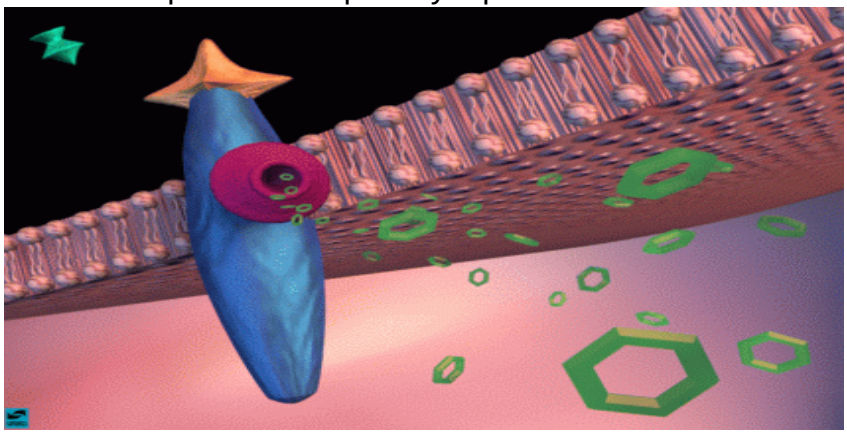
Explain that cocaine concentrates in areas of the brain that are rich in dopamine synapses. Review dopamine transmission in the nucleus accumbens. Point to dopamine in the synapse and to dopamine bound to dopamine receptors and to uptake pumps on the terminal.

Cocaine binding to uptake pumps: inhibition of dopamine uptake



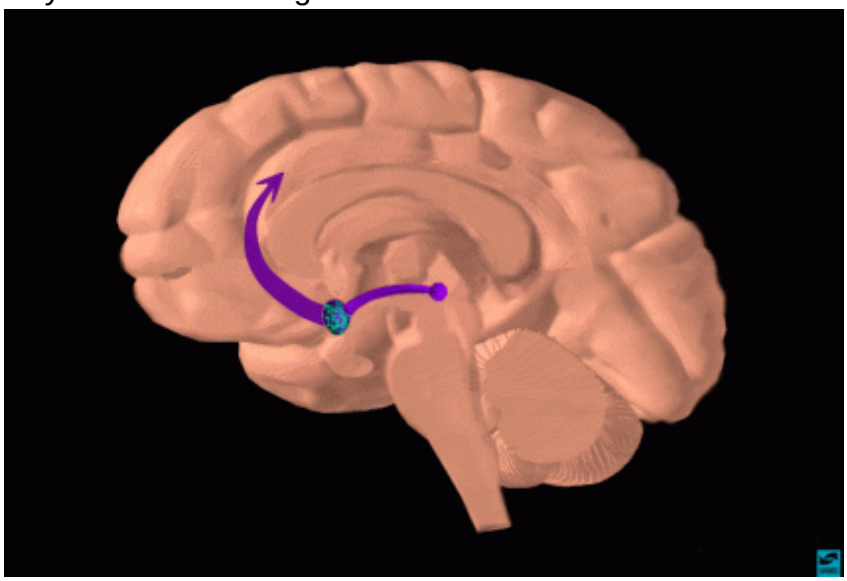
Now, show what happens when cocaine is present in the synapse. Cocaine (turquoise) binds to the uptake pumps and prevents them from removing dopamine from the synapse. This results in more dopamine in the synapse, and more dopamine receptors are activated.

Increased cAMP produced in post-synaptic cell



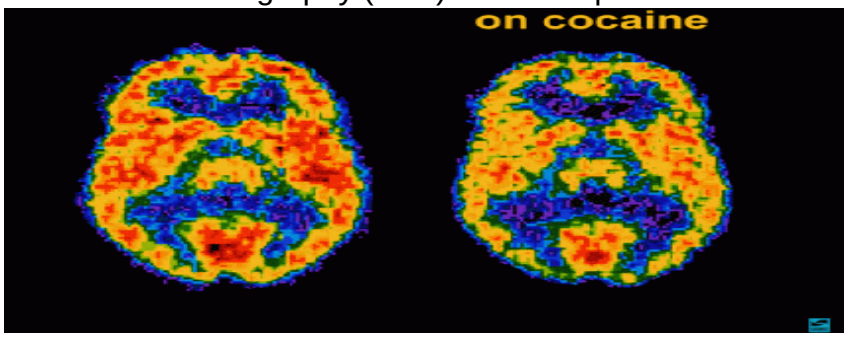
In a closer view, show how this affects the function of the cell. The increased activation of dopamine receptors causes increased production of cAMP inside the post-synaptic cell. This causes many changes inside the cell that lead to abnormal firing patterns.

Summary - cocaine binding in nucleus accumbens and activation of reward pathway



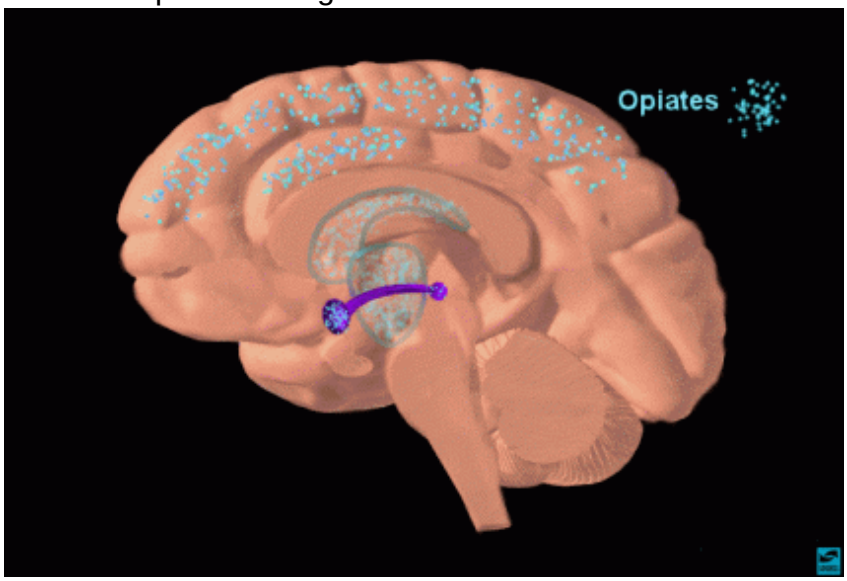
Show the "big picture," As a result of cocaine's actions in the nucleus accumbens (point to the sprinkles of cocaine in the nuc. acc.), there are increased impulses leaving the nucleus accumbens to activate the reward system. Indicate that with continued use of cocaine, the body relies on this drug to maintain rewarding feelings. The person is no longer able to feel the positive reinforcement or pleasurable feelings of natural rewards (food, water, sex).

Positron emission tomography (PET) scan of a person on cocaine



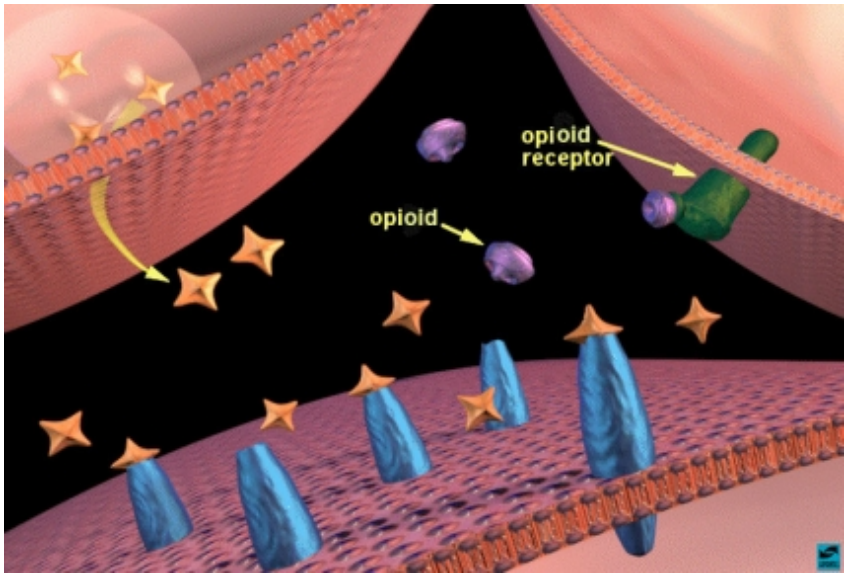
Cocaine has other actions in the brain in addition to activating reward. Scientists have the ability to see how cocaine actually affects brain function in people. The PET scan allows one to see how the brain uses glucose; glucose provides energy to each neuron so it can perform work. The scans show where the cocaine interferes with the brain's use of glucose - or its metabolic activity. The left scan is taken from a normal, awake person. The red color shows the highest level of glucose utilization (yellow represents less utilization and blue shows the least). The right scan is taken from a cocaine abuser on cocaine. It shows that the brain cannot use glucose nearly as effectively - show the loss of red compared to the left scan. There are many areas of the brain that have reduced metabolic activity. The continued reduction in the neurons' ability to use glucose (energy) results in disruption of many brain functions.

Localization of opioid binding sites



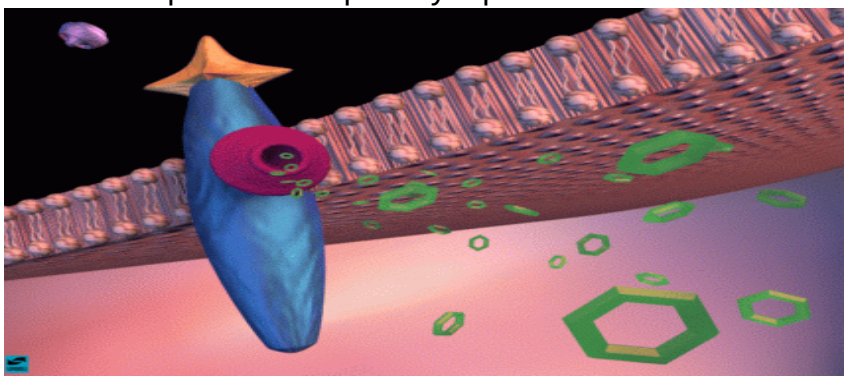
When a person injects heroin or morphine, it too, travels quickly to the brain. Point to the areas where opioids concentrate. The VTA, nucleus accumbens, caudate nucleus and thalamus are highlighted. The opioids bind to opioid receptors that are concentrated in areas within the reward system. Indicate that the action of opioids in the thalamus contributes to their ability to produce analgesia.

Opioids binding to opioid receptors in the nucleus accumbens: increased dopamine release



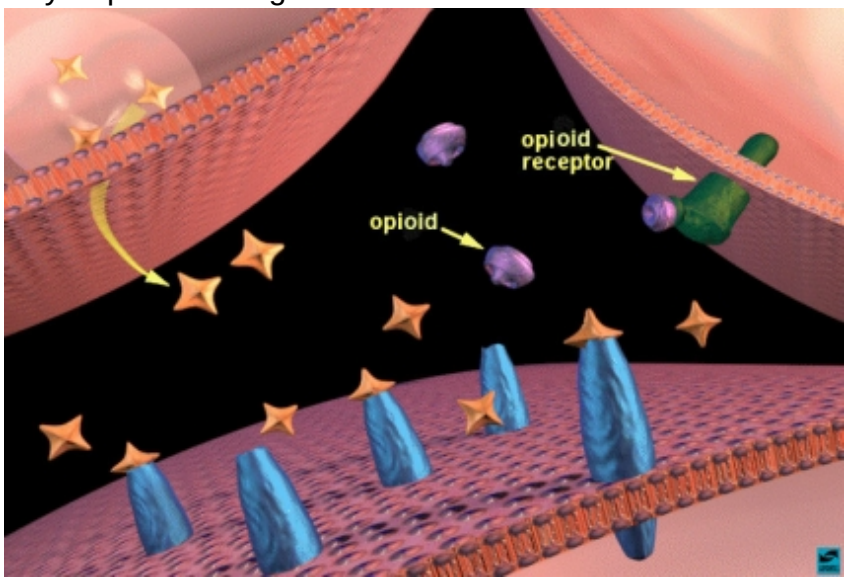
Show how opioids activate the reward system using the nucleus accumbens as an example. Explain that the action is a little more complicated than cocaine's because more than two neurons are involved. Point out that 3 neurons participate in opioid action; the dopamine terminal, another terminal (on the right) containing a different neurotransmitter (probably GABA for those that would like to know), and the post-synaptic cell containing dopamine receptors. Show that opioids bind to opioid receptors (green) on the neighboring terminal and this sends a signal to the dopamine terminal to release more dopamine. [In case an inquisitive student asks how - one theory is that opioid receptor activation decreases GABA release, which normally inhibits dopamine release - so dopamine release is increased.]

Increased cAMP produced in post-synaptic cell



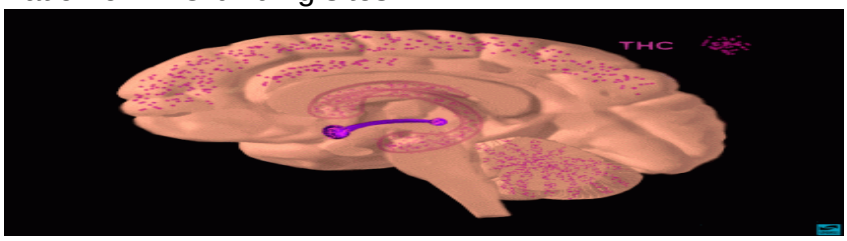
In a closer view, again, show how this affects the function of the post-synaptic cell. Since there is more dopamine released, there is increased activation of dopamine receptors, similar to the effect of cocaine. This causes increased production of cAMP inside the post-synaptic cell, which alters the normal activity of the neuron.

Summary - opioid binding in nucleus accumbens and activation of the reward pathway



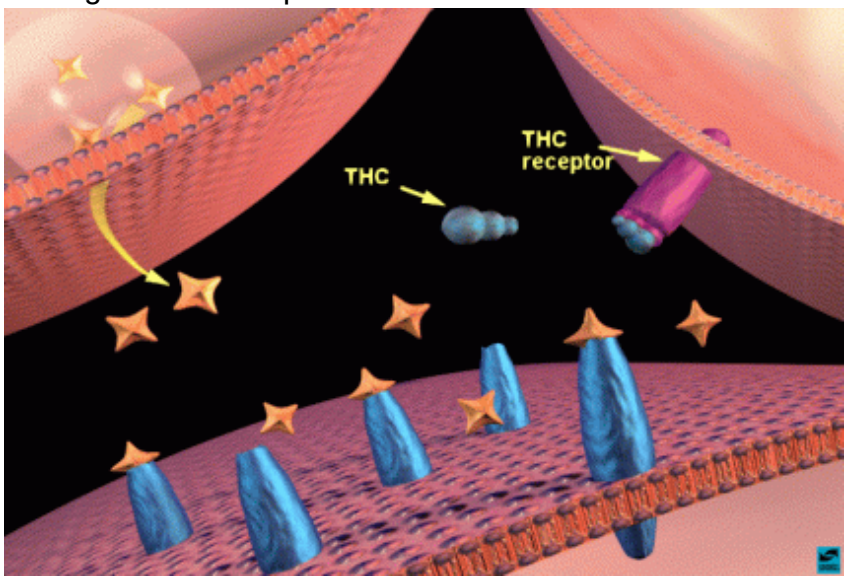
Show the "big picture". As a result of opioid actions in the nucleus accumbens (point to the sprinkles of opioids in the nuc. acc.), there are increased impulses leaving the nucleus accumbens to activate the reward system (point to the frontal cortex). As with cocaine, continued use of opioids makes the body rely on the presence of the drug to maintain rewarding feelings and other normal behaviors. The person is no longer able to feel the benefits of natural rewards (food, water, sex) and can't function normally without the drug present.

Localization of THC binding sites



When a person smokes marijuana, the active ingredient, THC, travels quickly to the brain. Point to the areas where THC (magenta) concentrates. The VTA, nucleus accumbens, caudate nucleus, hippocampus, and cerebellum are highlighted. THC binds to cannabinoid receptors that are concentrated in areas within the reward system as well as these other areas. Indicate that the action of THC in the hippocampus explains its ability to interfere with memory and actions in the cerebellum are responsible for its ability to cause incoordination and loss of balance. Just as the body produces and responds to its own opioids (endorphins), the body produces and responds to its own cannabinoid molecules, called endocannabinoids. THC interacts with the body's endocannabinoid signaling system.

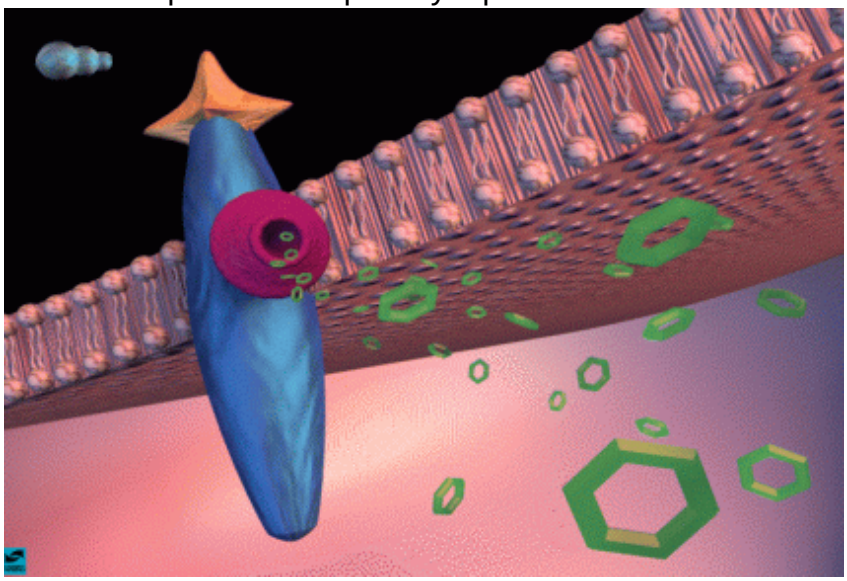
THC binding to THC receptors in the nucleus accumbens: increased dopamine release



Over the last few decades, there has been intense study to learn about the endocannabinoid system, not only because of the popularity of marijuana as a recreational drug but also because of the increased use of marijuana for medical purposes. THC is thought to act in a similar way to opioids. Again, use the nucleus accumbens as an example. The same 3 neurons are probably involved; the dopamine terminal, another terminal (on the right) containing a different neurotransmitter (GABA), and the post-synaptic cell containing dopamine receptors. Ask the students if they can tell you how THC might work. THC binds to THC receptors (magenta) on the neighboring terminal and this inhibits the GABA signal, which causes the dopamine terminal to

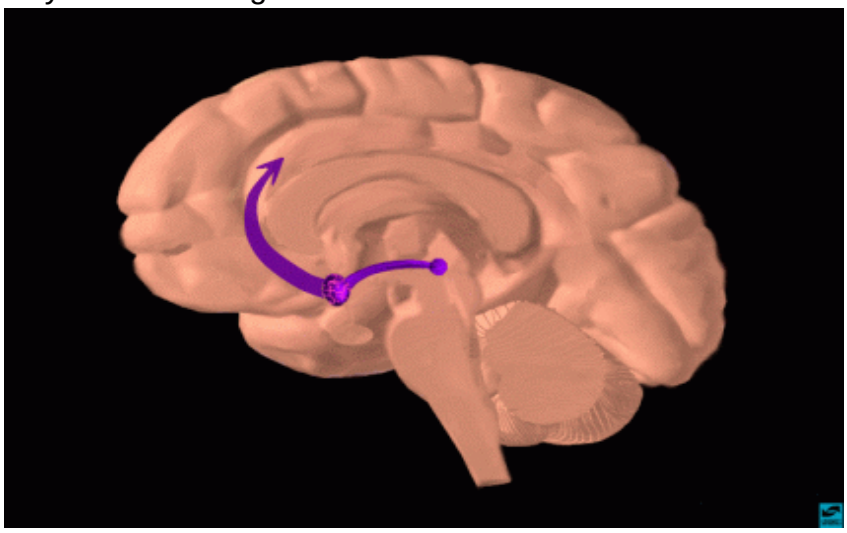
release more dopamine.

Increased cAMP produced in post-synaptic cell



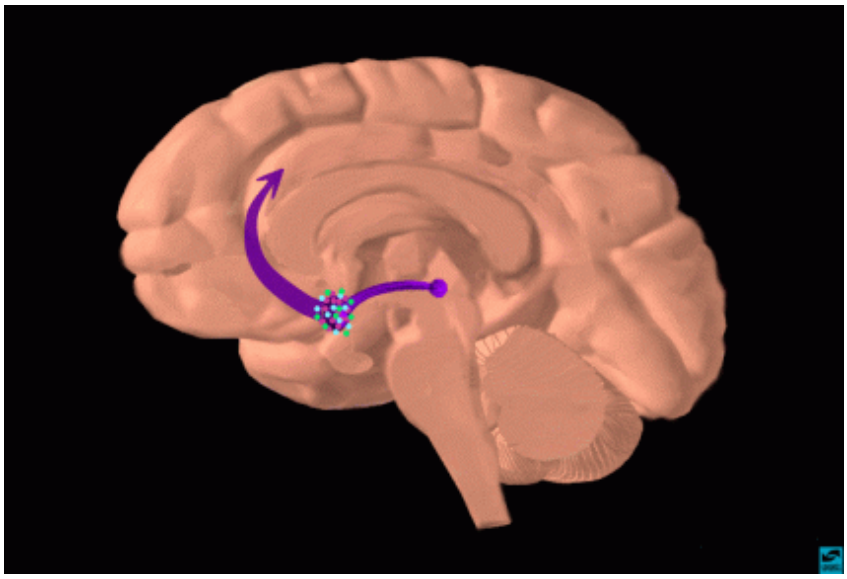
In a closer view, show how this affects the function of the post-syanaptic cell. Since there is more dopamine released, there is increased activation of dopamine receptors. This causes increased production of cAMP inside the post-synaptic cell which alters the normal activity of the neuron.

Summary - THC binding in nucleus accumbens and activation of the reward pathway



Show the "big picture." As a result of THC actions in the nucleus accumbens (point to the concentration of THC in the nuc. acc.), there are increased impulses leaving the nucleus accumbens to activate the reward system (point to the frontal cortex). Scientists still don't know how the continued use of marijuana alters the reward system. Indicate that this is an area of intense research by neuroscientists.

Overall summary - these drugs of abuse all activate the reward system via increasing dopamine neurotransmission



In this last slide, the binding of all 3 drugs is shown in one of the reward areas, the nucleus accumbens. Summarize that each drug increases the activity of the reward pathway by increasing dopamine transmission. This happens even though the drugs act by different mechanisms. Because of the way our brains are designed, and because these drugs activate a particular brain pathway for reward, they have the ability to be misused.

Start a discussion; ask the students if they can think of any other drugs that are misused that probably activate the reward system in the same way. Answer: alcohol, nicotine, and amphetamine are good examples.

Additional Guidance

Background Information for the Presenter

Objectives

The objective of the teaching packet is to inform students (high school) how 3 drugs of abuse (cocaine, opiates, marijuana) actually work in the brain. The packet is arranged in 3 sections. The first section introduces the brain and presents some basic neurobiology, the second introduces the reward pathway and the third presents the mechanism of action of each drug and how each affects the reward system.

Before Entering the Classroom

- Arrange to talk with the teacher (by telephone or in person).
- Obtain information on the age group and extent of biology background.
- Discuss the subjects that you will present to the class.
- If possible, meet with the teacher & review the presentation; provide teacher with some background material if requested.
- Solicit advice from the teacher about teaching strategies (e.g. what to do if some students are disruptive or not listening).
- Read the narrative script and practice the presentation - this is different from a scientific seminar to peers!

Once in the Classroom

- Introduce yourself to the class.
- Talk briefly about your path to your current job.
- Describe what you do (simply).
- Indicate the object of your presentation.
- Invite questions during your presentation.
- If the opportunity arises, ask questions of the students.
- Be prepared to define any words you use.

General Instructions

- The presentation should take approximately 30-40 minutes (without questions); it can be presented in 2 class sessions if so desired.
- Use the narrative text as a guide, it need not be repeated word-for-word.

The Neurobiology of Drug Addiction

The second in a 5-part series, explores the science behind addiction, describing the brain and reward center, and the action of heroine and cocaine.

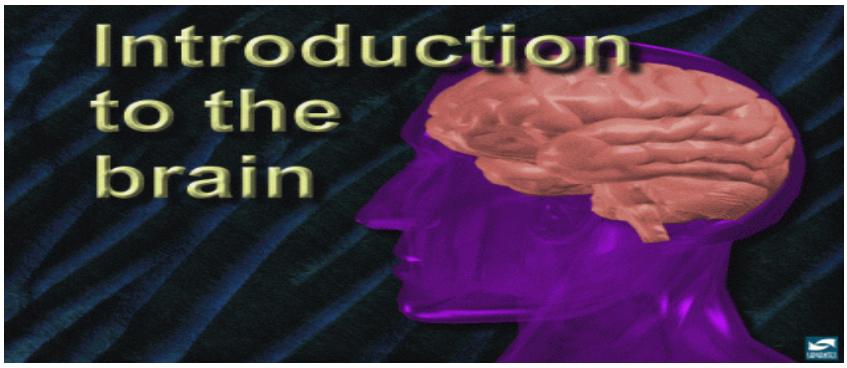
The objective of the presentation is to illustrate to the audience the basic function of the brain, the neurobiological basis for addiction and the actions of heroin and cocaine. The presentation is arranged in 4 sections. The first section introduces the brain and presents some basic neurobiology, the second introduces the reward pathway and the third and fourth present the mechanism of action of heroin and cocaine and how each affects the reward system.

This presentation can be downloaded as a Powerpoint file - The Neurobiology of Drug Addiction (PPT, 4.3MB) and was last reviewed in November, 2019

Expand All

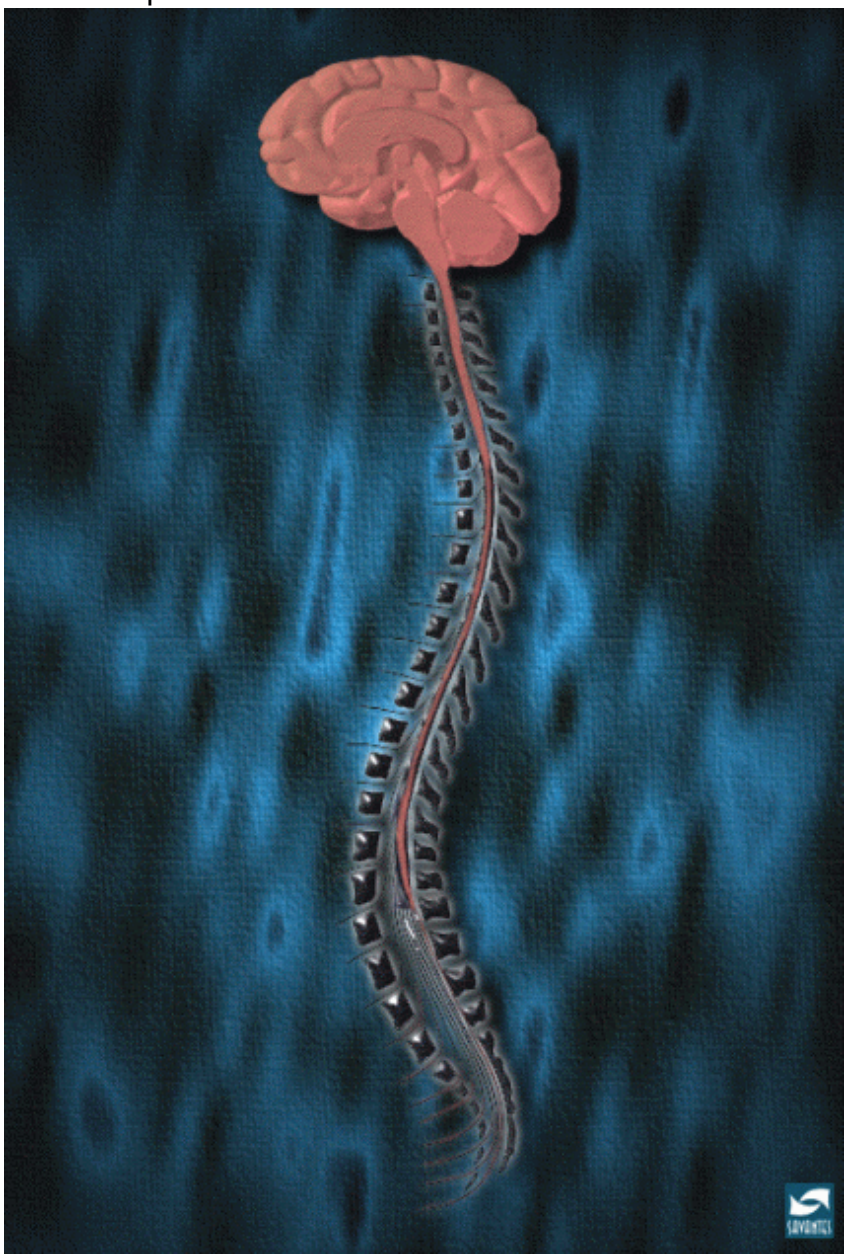
Introduction to the Brain

Introduction



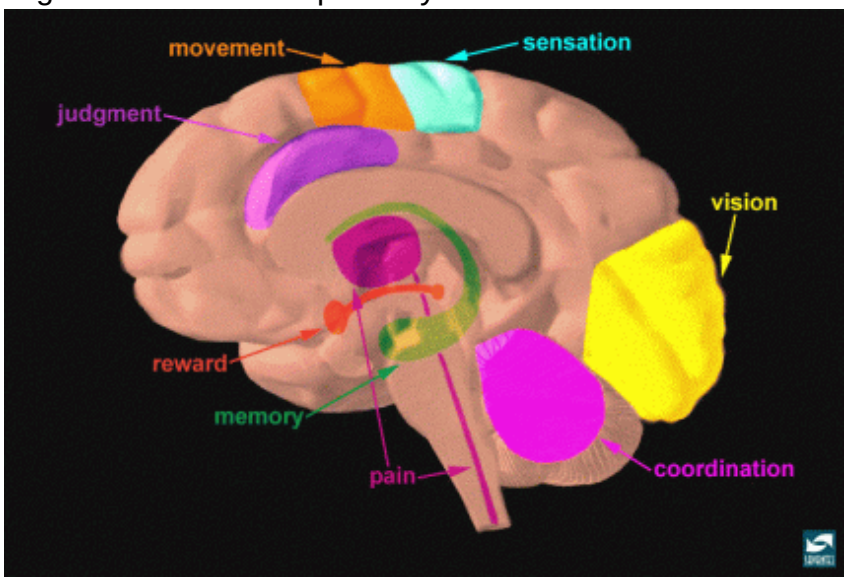
Introduce the purpose of your presentation. Indicate that you will explain how the brain basically works and how and where drugs such as heroin and cocaine work in the brain. Tell your audience that you will discuss the concept of "reward" which is the property that is characteristic of many addictive drugs.

The brain and spinal cord



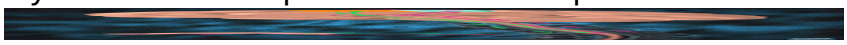
The central nervous system is composed of both the brain and the spinal cord. Describe the brain as a functional unit; it is made up of billions of nerve cells (neurons) that communicate with each other using electrical and chemical signals.

Brain regions and neuronal pathways



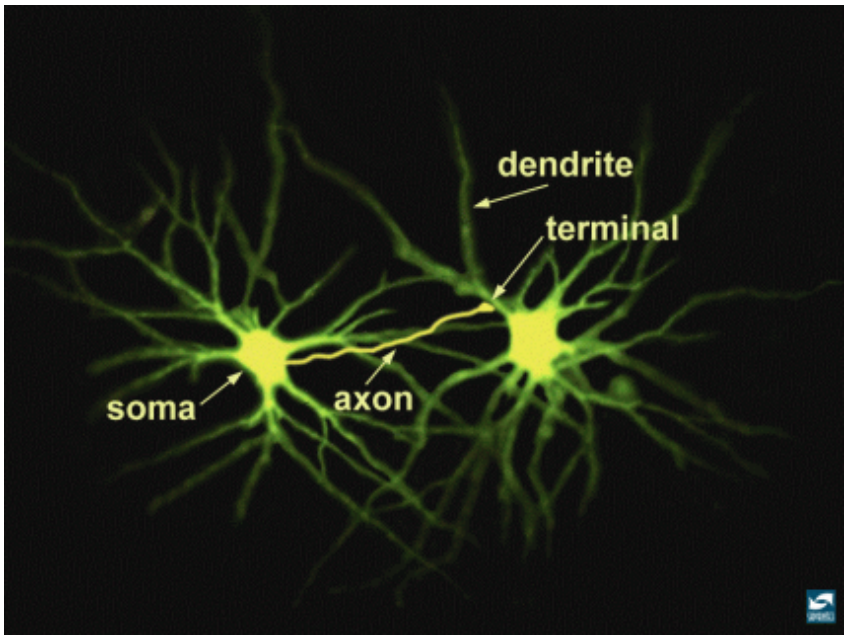
Certain parts of the brain govern specific functions. Point to areas such as the sensory (blue), motor (orange) and visual cortex (yellow) to highlight their specific functions. Point to the cerebellum (pink) for coordination and to the hippocampus (green) for memory. Indicate that nerve cells or neurons connect one area to another via pathways to send and integrate information. The distances that neurons extend can be short or long. For example, point to the reward pathway (deep orange). Explain that this pathway is activated when a person receives positive reinforcement for certain behaviors ("reward"). Indicate that you will explain how this happens when a person takes an addictive drug. As another example, point to the thalamus (magenta). This structure receives information about pain coming from the body (magenta line within the spinal cord), and passes the information up to the cortex. Tell the audience that you can look at this in more detail.

Pathway for sensation of pain and reaction to pain



This is a long pathway, in which neurons make connections in both the brain and the spinal cord. Explain what happens when one slams a door on one's finger. First, nerve endings in the finger sense the injury to the finger (sensory neurons) and they send impulses along axons to the spinal cord (magenta pathway). Point to each part of the pathway as you explain the flow of information. The incoming axons form a synapse with neurons that project up to the brain. The neurons that travel up the spinal cord then form synapses with neurons in the thalamus, which is a part of the midbrain (magenta circle). The thalamus organizes this information and sends it to the sensory cortex (blue), which interprets the information as pain and directs the nearby motor cortex (orange) to send information back to the thalamus (green pathway). Again, the thalamus organizes this incoming information and sends signals down the spinal cord, which direct motor neurons to the finger and other parts of the body to react to the pain (e.g., shaking the finger or screaming "ouch!").

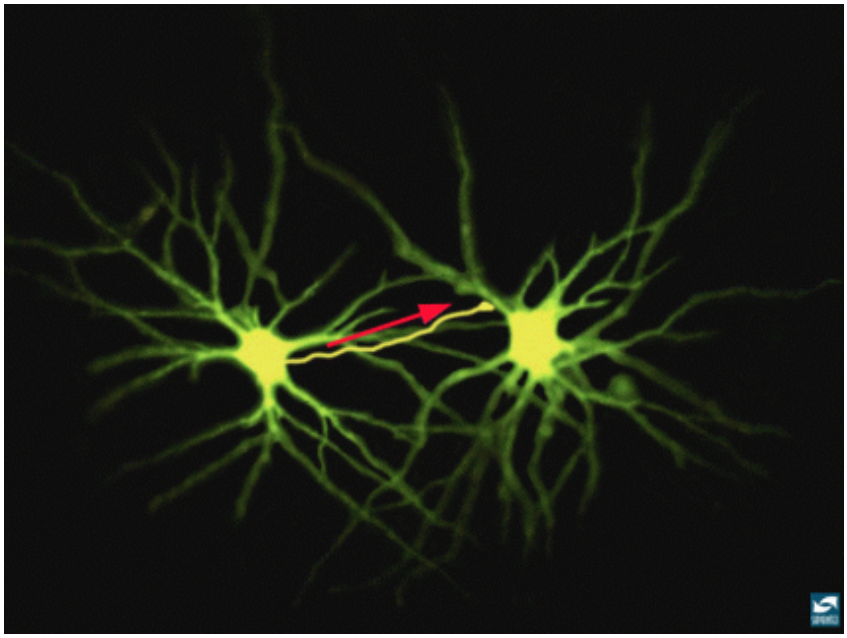
Neuronal structure



Indicate that these pathways are made up of neurons. This image contains real neurons from the thalamus. They have been filled with a fluorescent dye and viewed through a microscope. Describe the anatomy of a neuron: point to the cell body (soma), dendrites, and axon (marked with text). At the end of the axon is the terminal, which makes a connection with another neuron.

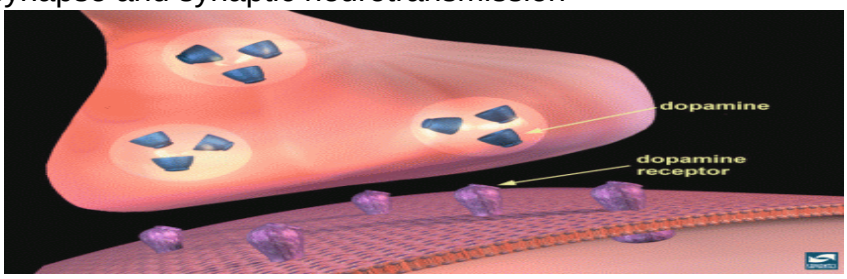
[Note: the axon has been drawn in for clarity, but actually, the axons of these neurons travel to the cerebral cortex.]

Impulse flow



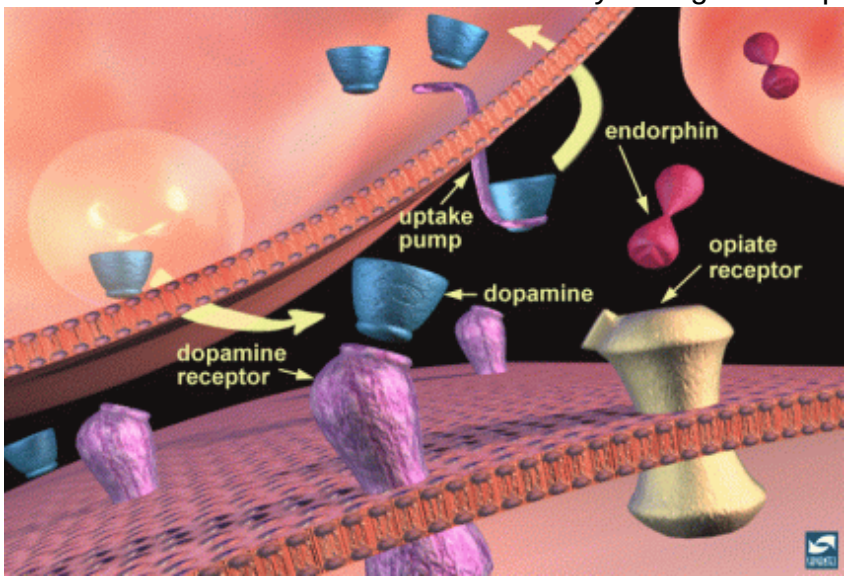
Explain the normal direction of the flow of information (electrical and chemical). An electrical impulse (the action potential) travels down the axon toward the terminal. Point to the terminal. The terminal makes a connection with the dendrite of neighboring neuron, where it passes on chemical information. The area of connection is called the synapse. Although the synapse between a terminal and a dendrite (shown here) is quite typical, other types of synapses exist as well. For example, a synapse can occur between a terminal and a soma or axon.

The synapse and synaptic neurotransmission



Describe the synapse and the process of chemical neurotransmission. As an electrical impulse arrives at the terminal, it triggers vesicles containing a neurotransmitter, such as dopamine (in blue), to move toward the terminal membrane. The vesicles fuse with the terminal membrane to release their contents (in this case, dopamine). Once inside the synaptic cleft (the space between the two neurons) the dopamine can bind to specific proteins called dopamine receptors (in pink) on the membrane of a neighboring neuron. This is illustrated in more detail on the next image.

Dopamine neurotransmission and modulation by endogenous opiates

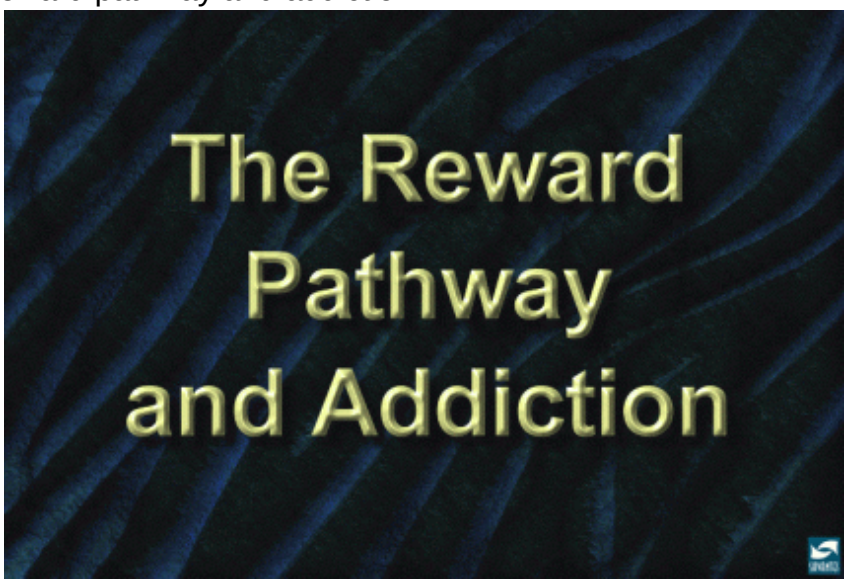


Using the close-up of a synapse, continue using dopamine for your example of synaptic function. Explain that it is synthesized in the nerve terminal and packaged in vesicles. Reiterate the steps in neurotransmission. Show how the vesicle fuses with the membrane and releases dopamine. The dopamine molecules can then bind to a dopamine receptor (in pink). After the dopamine binds, it comes off the receptor and is removed from the synaptic cleft by uptake pumps (also proteins) that reside on the terminal (arrows show the direction of movement). This process is important because it ensures that not too much dopamine remains in the synaptic cleft at any one time. Also point out that there are neighboring neurons that release another compound called a neuromodulator. Neuromodulators help to enhance or inhibit neurotransmission that is controlled by neurotransmitters such as dopamine. In this case, the neuromodulator is an

"endorphin" (in red). Endorphins bind to opiate receptors (in yellow) which can reside on the post-synaptic cell (shown here) or, in some cases, on the terminals of other neurons (this is not shown so it must be pointed out). The endorphins are destroyed by enzymes rather than removed by uptake pumps

The Reward Pathway and Addiction

The reward pathway and addiction

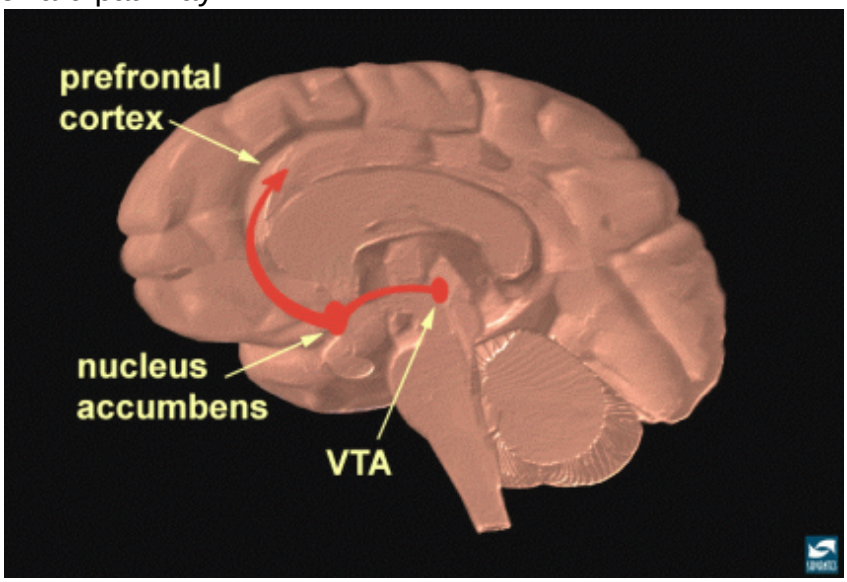


Introduce the concept of reward. Humans, as well as other organisms engage in behaviors that are rewarding; the pleasurable feelings provide positive reinforcement so that the behavior is repeated. There are natural rewards as well as artificial rewards, such as drugs.

Natural rewards

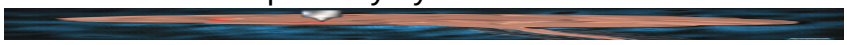
Natural rewards such as food, water, sex and nurturing allow the organism to feel pleasure when eating, drinking, procreating and being nurtured. Such pleasurable feelings reinforce the behavior so that it will be repeated. Each of these behaviors is required for the survival of the species. Remind your audience that there is a pathway in the brain that is responsible for reinforcing rewarding behaviors. This can be viewed in more detail in the next slide.

The reward pathway



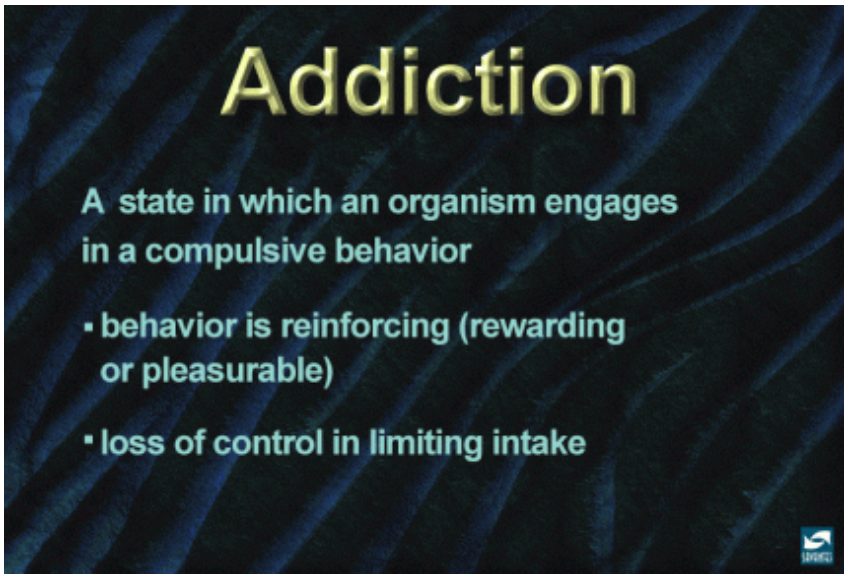
Tell your audience that this is a view of the brain cut down the middle. An important part of the reward pathway is shown and the major structures are highlighted: the ventral tegmental area (VTA), the nucleus accumbens, and the prefrontal cortex. The VTA is connected to both the nucleus accumbens and the prefrontal cortex via this pathway and it sends information to these structures via its neurons. The neurons of the VTA contain the neurotransmitter dopamine, which is released in the nucleus accumbens and in the prefrontal cortex (point to each of these structures). Reiterate that this pathway is activated by a rewarding stimulus. [Note: the pathway shown here is not the only pathway activated by rewards, other structures are involved too, but only this part of the pathway is shown for simplicity.]

Activation of the reward pathway by an electrical stimulus



The discovery of the reward pathway was achieved with the help of animals such as rats. Rats were trained to press a lever for a tiny electrical jolt to certain parts of the brain. Show that when an electrode is placed in the nucleus accumbens, the rat keeps pressing the lever to receive the small electrical stimulus because it feels pleasurable and that positive feeling is reinforced by the release of dopamine in that brain area. Point to an area of the brain close to the nucleus accumbens. Tell the audience that when the electrode is placed there, the rat will not press the lever for the electrical stimulus because stimulating neurons in a nearby area that does not connect with the nucleus accumbens does not activate the reward pathway. The importance of the neurotransmitter dopamine has been determined in these experiments because scientists can measure an increased release of dopamine in the reward pathway after the rat receives the reward. And, if the dopamine release is prevented (either with a drug or by destroying the pathway), the rat won't press the bar for the electrical jolt. So, with the help of the rats, scientists figured out the specific brain areas as well as some of the neurochemicals involved in the reward pathway.

Addiction

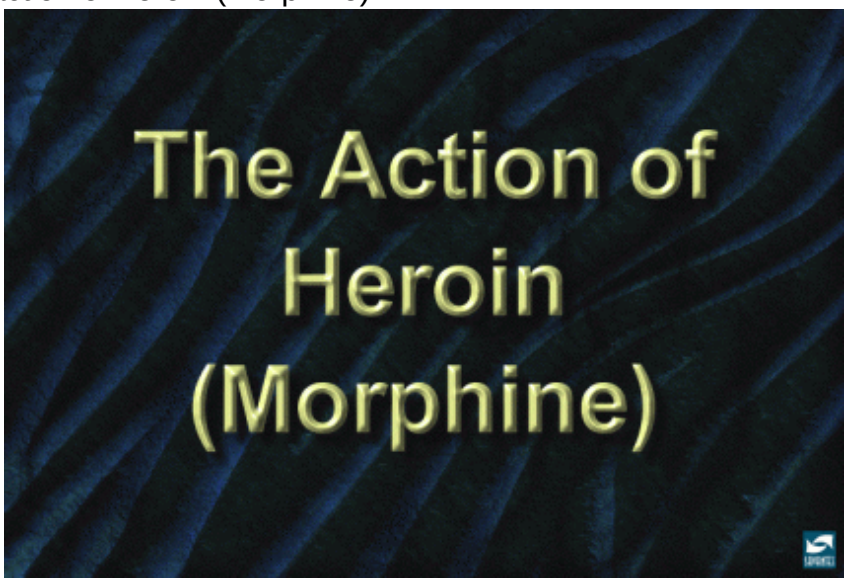


Now that you have defined the concept of reward, you can define addiction. Addiction is a state in which an organism engages in a compulsive behavior, even when faced with negative consequences. This behavior is reinforcing, or rewarding, as you have just discussed. A major

feature of addiction is the loss of control in limiting intake of the addictive substance. The most recent research indicates that the reward pathway may be even more important in the craving associated with addiction, compared to the reward itself. Scientists have learned a great deal about the biochemical, cellular, and molecular bases of addiction; it is clear that addiction is a disease of the brain. State that you will provide two examples of the interaction between drugs that are addictive, their cellular targets in the brain, and the reward pathway.

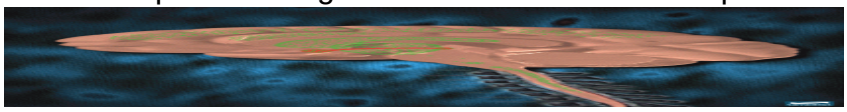
The Action of Heroin (Morphine)

The action of heroin (morphine)



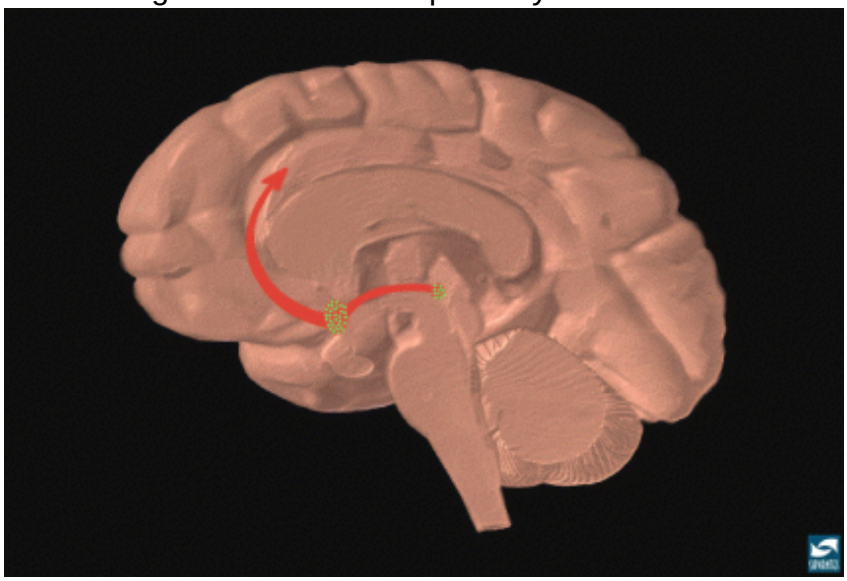
Heroin is an addictive drug, although not all users become addicted. Environment and the personality of the user are important in producing addiction. Heroin produces euphoria or pleasurable feelings and can be a positive reinforcer by interacting with the reward pathway in the brain. Indicate that you will explain how this happens.

Localization of opioid binding sites within the brain and spinal cord



When a person injects heroin (or morphine), the drug travels quickly to the brain through the bloodstream. Actually, heroin can reach the brain just as quickly if it is smoked (see description of slide #25). Users also snort heroin to avoid problems with needles. In this case, the heroin doesn't reach the brain as quickly as if it were injected or smoked, but its effects can last longer. Once in the brain, the heroin is converted to morphine by enzymes; the morphine binds to opioid receptors in certain areas of the brain. Point to the areas where opioids bind (green dots). Part of the cerebral cortex, the VTA, nucleus accumbens, thalamus, brainstem and spinal cord are highlighted. Show that the morphine binds to opioid receptors that are concentrated in areas within the reward pathway (including the VTA, nucleus accumbens and cortex). Morphine also binds to areas involved in the pain pathway (including the thalamus, brainstem and spinal cord). Binding of morphine to areas in the pain pathway leads to analgesia.

Morphine binding within the reward pathway

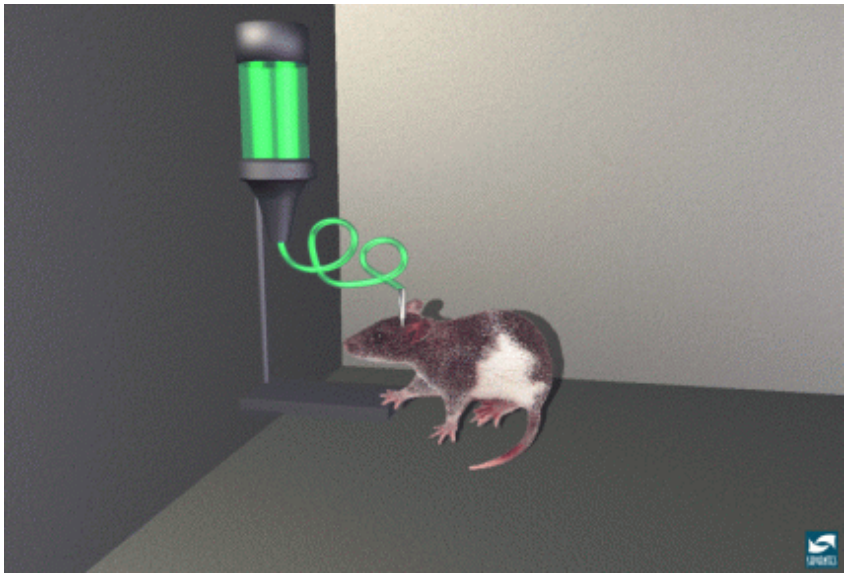


Reiterate that morphine binds to receptors on neurons in the VTA and in the nucleus accumbens. This is shown here within the reward pathway. Indicate that you will show how morphine activates this pathway on the next image.

Opioids binding to opioid receptors in the nucleus accumbens: increased dopamine release

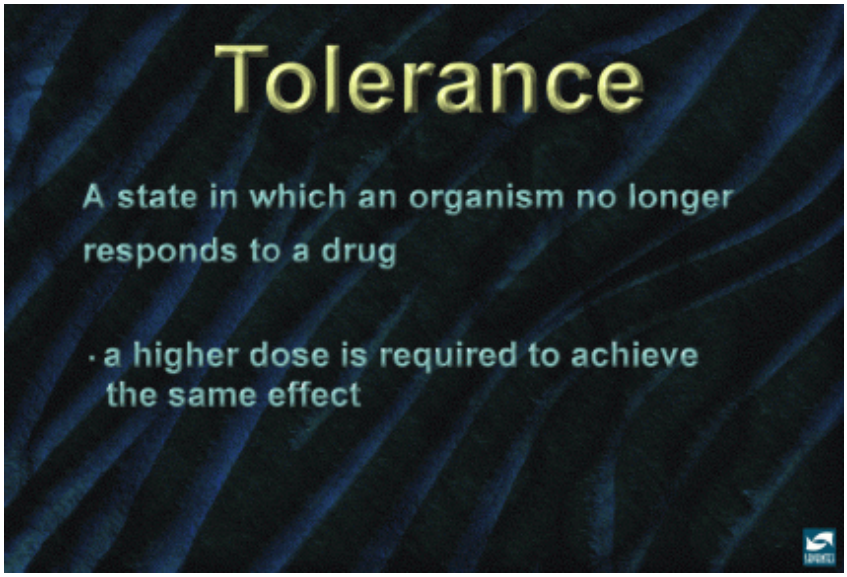
This is a close-up view of a synapse in the nucleus accumbens. Three types of neurons participate in opioids' action; one that releases dopamine (on the left), a neighboring terminal (on the right) containing a different neurotransmitter (probably GABA for those who would like to know), and the post-synaptic cell containing dopamine receptors (in pink). Show that opioids bind to opioid receptors (yellow) on the neighboring terminal and this sends a signal to the dopamine terminal to release more dopamine. [In case someone asks how--one theory is that opioid receptor activation decreases GABA release, which normally inhibits dopamine release--so dopamine release is increased.]

Rats self-administer heroin



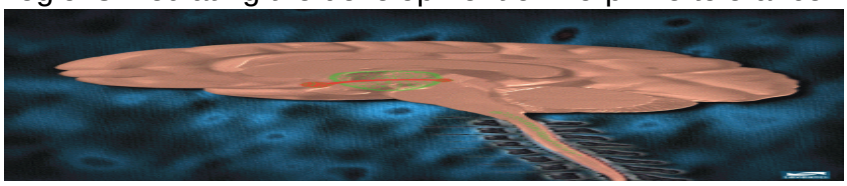
Just as a rat will stimulate itself with a small electrical jolt (into the reward pathway), it will also press a bar to receive heroin. In this image, the rat is self-administering heroin through a small needle placed directly into the nuclues accumbens. The rat keeps pressing the bar to get more heroin because the drug makes the rat feel good. The heroin is positively reinforcing and serves as a reward. If the injection needle is placed in an area nearby the nucleus accumbens, the rat won't self-administer the heroin. Scientists have found that dopamine release is increased within the reward pathway of rats self-administering heroin. Increased dopamine in this circuit reinforces the behavior of taking the drug—essentially "teaching" the brain to repeat the action.

Definition of tolerance



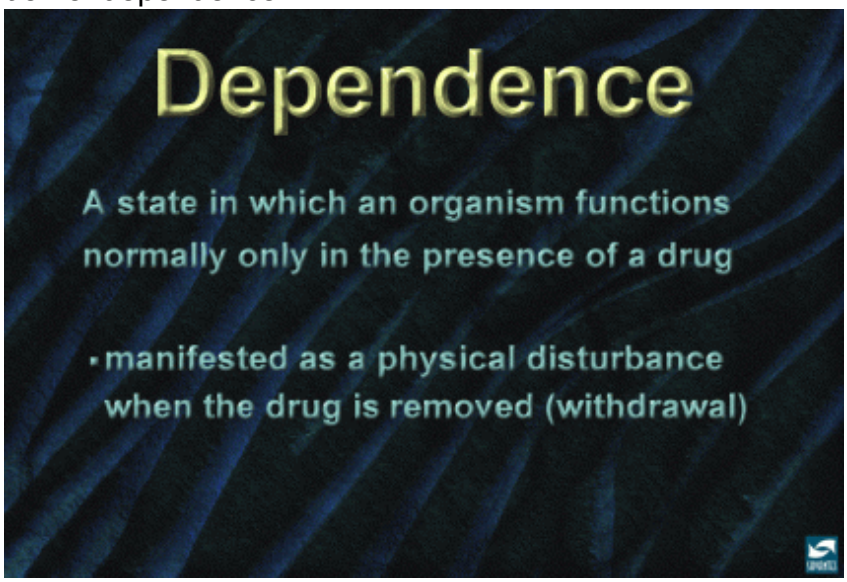
When drugs such as heroin are used repeatedly over time, tolerance may develop. Tolerance occurs when the person no longer responds to the drug in the way that person initially responded. Stated another way, it takes a higher dose of the drug to achieve the same level of response achieved initially. So, for example, in the case of heroin or morphine, tolerance develops rapidly to the analgesic and other effects of the drug. [The development of tolerance is not addiction, although many drugs that produce tolerance also have addictive potential.] Tolerance to drugs can be produced by several different mechanisms, but in the case of morphine or heroin, tolerance develops at the level of the cellular targets. For example, when morphine binds to opioid receptors, it triggers the inhibition of an enzyme (adenylate cyclase) that orchestrates several chemicals in the cell to maintain the firing of impulses. After repeated activation of the opioid receptor by morphine, the enzyme adapts so that the morphine can no longer cause changes in cell firing. Thus, the effect of a given dose of morphine or heroin is diminished.

Brain regions mediating the development of morphine tolerance



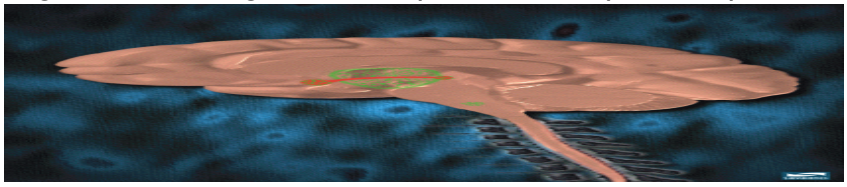
The development of tolerance to the analgesic effects of morphine involves different areas of the brain separate from those in the reward pathway. Point to the two areas involved here, the thalamus, and the spinal cord (green dots). Both of these areas are important in sending pain messages and are responsible for the analgesic effects of morphine. The parts of the reward pathway involved in heroin or morphine addiction are shown for comparison.

Definition of dependence



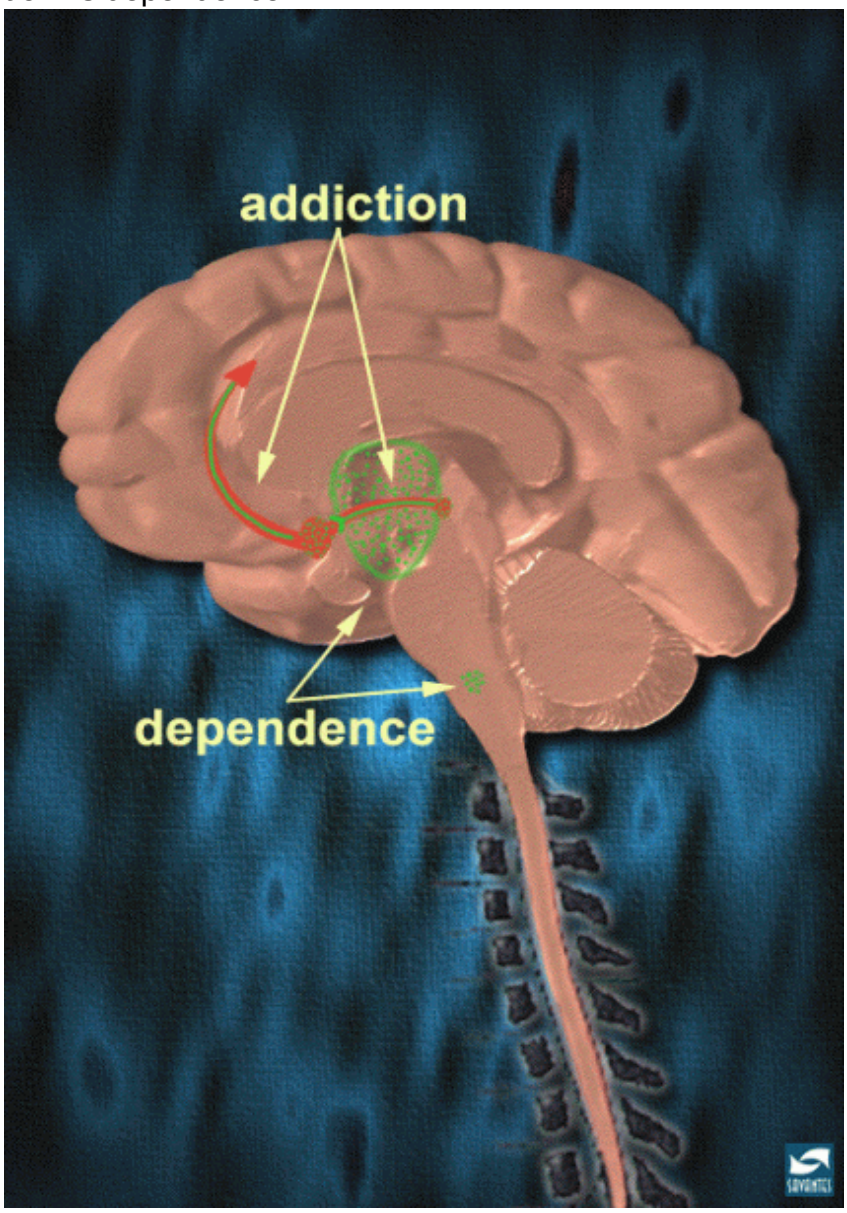
With repeated use of heroin, dependence also occurs. Dependence develops when the neurons adapt to the repeated drug exposure and only function normally in the presence of the drug. When the drug is withdrawn, several physiologic reactions occur. These can be mild (e.g. for caffeine) or even life threatening (e.g. for alcohol). This is known as the withdrawal syndrome. In the case of heroin, withdrawal can be very serious, and the user will seek and take the drug again to avoid the withdrawal syndrome.

Brain regions mediating the development of morphine dependence



The development of dependence to morphine also involves specific areas of the brain, separate from the reward pathway. In this case, point to the thalamus and the brainstem (green dots). The parts of the reward pathway involved in heroin (morphine) addiction are shown for comparison. Many of the withdrawal symptoms from heroin or morphine are generated when the opioid receptors in the thalamus and brainstem are deprived of the drug.

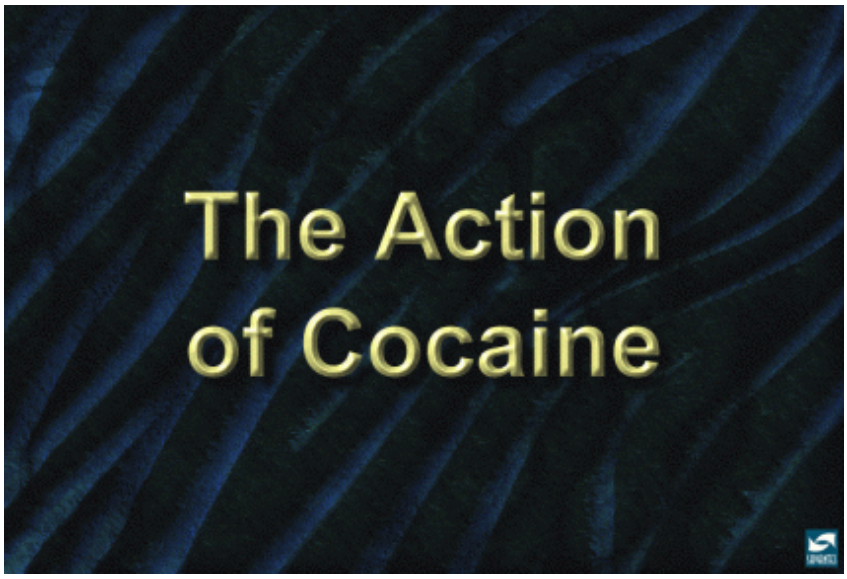
Addiction vs dependence



As you have just explained, different parts of the brain are responsible for the addiction and dependence to heroin and opioids. Review the areas in the brain underlying the addiction to morphine (reward pathway) and those underlying the dependence to morphine (thalamus and brainstem). Thus, it is possible to be dependent on morphine, without being addicted to morphine. (Although, if one is addicted, they are most likely dependent as well.) This is especially true for people being treated chronically with morphine for pain, for example associated with terminal cancer. They may be dependent--if the drug is stopped, they suffer a withdrawal syndrome. But most such patients are not compulsive users of the morphine, and they are not addicted. However, a proportion of people treated with morphine in the hospital for pain control after surgery may become addicted.

The Action of Cocaine

The action of cocaine

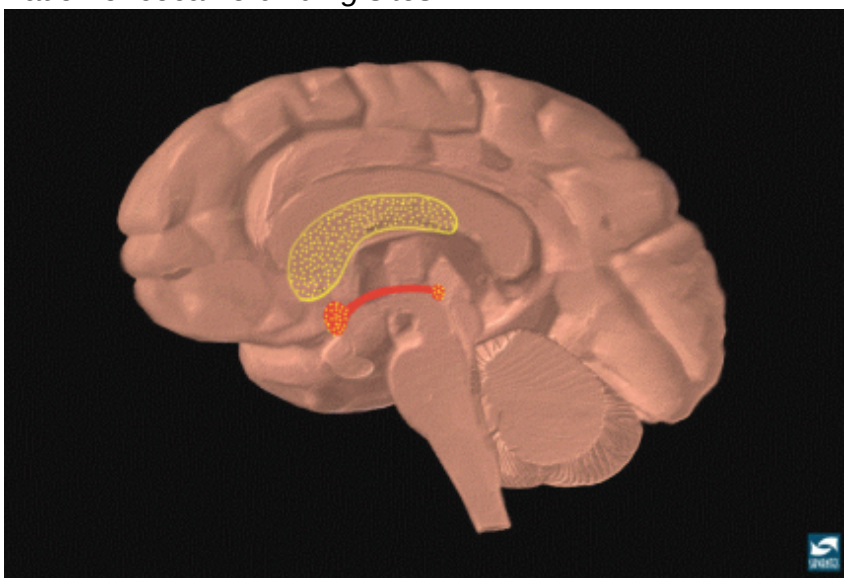


Cocaine is also an addictive drug, although like heroin, not all users become addicted.

Snorting vs smoking cocaine: different addictive liabilities

Cocaine is taken in two ways: snorting the powdered form (the hydrochloride salt) or smoking “crack” cocaine (the free base). Heating the hydrochloride salt form of cocaine will destroy it; the free base can be volatilized at high temperature without any destruction of the compound. Smoking gets the drug to the brain more quickly than does snorting. Show the audience why this happens. Snorting requires that the cocaine travels from the blood vessels in the nose to the heart (blue arrow), where it gets pumped to the lungs (blue arrow) to be oxygenated. The oxygenated blood (red arrows) carrying the cocaine then travels back to the heart where it is pumped out to the organs of the body, including the brain. However, smoking bypasses much of this--the cocaine goes from the lungs directly to the heart and up to the brain. The faster a drug with addictive liability reaches the brain, the more likely it will be misused. Thus, the time between taking the drug and the positive reinforcing or rewarding effects that are produced can determine the likelihood of misuse.

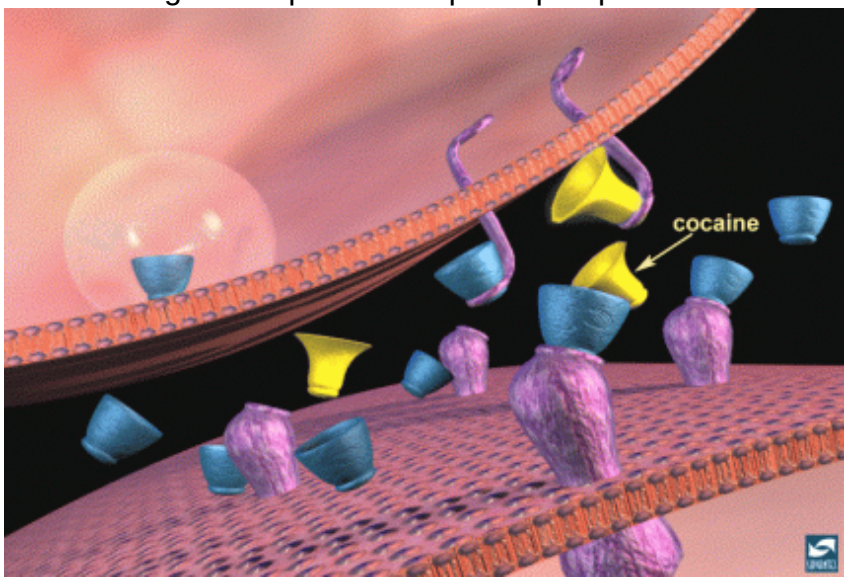
Localization of cocaine *binding sites*



When a person smokes or snorts cocaine, it reaches all areas of the brain, but it binds to sites in some very specific areas. These are highlighted with the yellow dots: the VTA, the nucleus accumbens, and the caudate nucleus (the largest structure). Point out that cocaine binds especially in the reward areas that you have just discussed. The binding of cocaine in other areas such as the caudate nucleus can explain other effects such as increased stereotypic (or

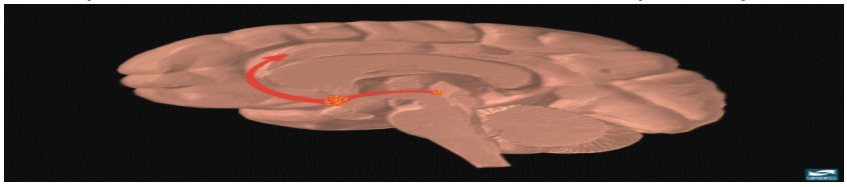
repetitive) behaviors (pacing, nail-biting, scratching, etc..)

Dopamine binding to receptors and uptake pumps in the nucleus accumbens: the action of cocaine



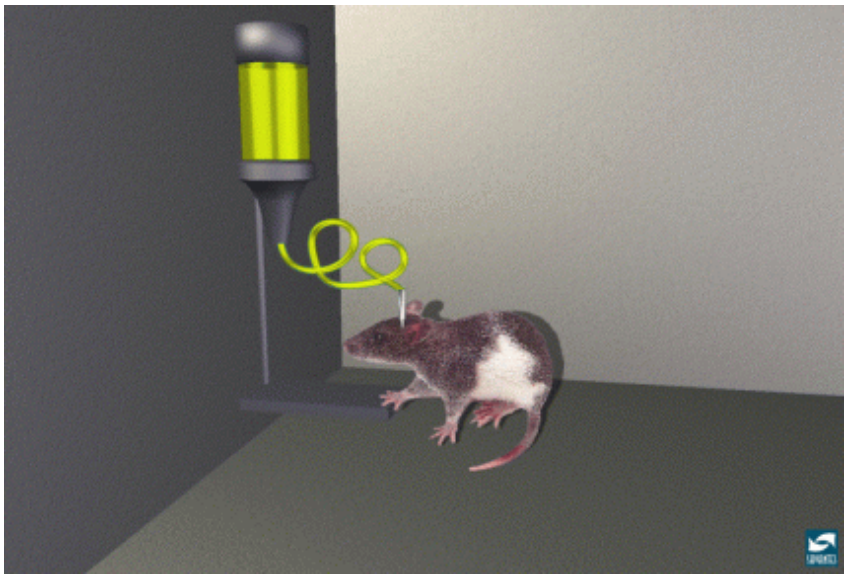
Explain that cocaine binds to sites in areas of the brain that are rich in dopamine synapses such as the VTA and the nucleus accumbens. Review dopamine transmission in the close-up of a synapse in the nucleus accumbens. Point to dopamine (inside the terminal) that is released into the synaptic space. The dopamine binds to dopamine receptors and then is taken up by uptake pumps back into the terminal. Now show what happens when cocaine is present (yellow). Cocaine binds to the uptake pumps and prevents them from transporting dopamine back into the neuron terminal. So more dopamine builds up in the synaptic space and it is free to activate more dopamine receptors. This is the same effect that you showed in an earlier image with morphine, where morphine increased dopamine release from the terminal to produce more dopamine in the synaptic space.

Cocaine dependence and activation of the reward pathway



Review where cocaine binds within the reward pathway (the VTA and the nucleus accumbens). As a result of cocaine's actions in the nucleus accumbens (point to the dots of cocaine in the VTA and nucleus accumbens), there are increased impulses leaving the nucleus accumbens to activate the reward system. This pathway can be activated even in the absence of cocaine (i.e., during craving). Indicate that with repeated use of cocaine, the body relies on this drug to maintain rewarding feelings. The person is no longer able to feel the positive reinforcement or pleasurable feelings of natural rewards (i.e. food, water, sex)--the person is only able to feel pleasure from the cocaine. Thus the user becomes dependent and when the cocaine is no longer present, anhedonia (inability to feel pleasure) and depression emerge as part of a withdrawal syndrome. To avoid this, the user goes back to the cocaine. Unlike the example for morphine, cocaine addiction (i.e., craving) and dependence (i.e., anhedonia) both involve structures in the reward pathway.

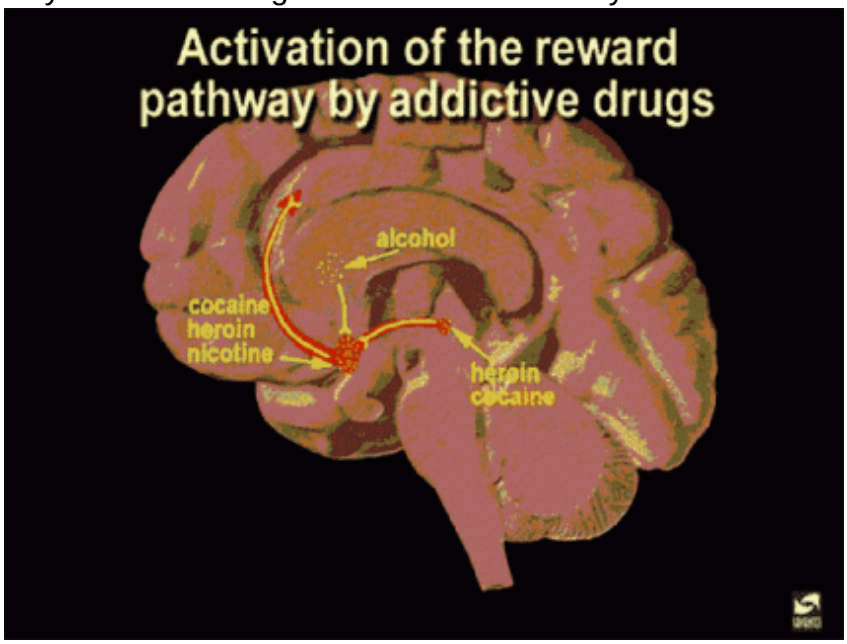
Rats self-administer cocaine



Scientists have measured increased dopamine levels in the synapses of the reward pathway in rats self-administering cocaine. Just as they did for heroin, rats will press a bar to receive injections of cocaine directly into areas of the reward pathway such as the nucleus accumbens and the VTA. Again, if the injection needle is placed near these regions (but not in them), the rat will not press the bar to receive the cocaine. The ability of rats to self-administer cocaine is an

excellent predictor of the addictive potential of this drug.

Summary - addictive drugs activate the reward system via increasing dopamine neurotransmission



In this last slide, the reward pathway is shown along with several drugs that have addictive potential. Just as heroin (morphine) and cocaine activate the reward pathway in the VTA and nucleus accumbens, other drugs such as nicotine and alcohol activate this pathway as well, although sometimes indirectly (point to the globus pallidus, an area activated by alcohol that connects to the reward pathway). While each drug has a different mechanism of action, each drug increases the activity of the reward pathway by increasing dopamine transmission. Because of the way our brains are designed, and because these drugs activate this particular brain pathway for reward, they have the ability to be misused. Thus, addiction is truly a disease of the brain. Effective medications now available to treat opioid addiction work by acting partly on the same reward pathway; in the future, medications may also be available to treat addiction to cocaine and other drugs in a similar way.

Additional Guidance

Background Information for the Presenter

Objectives

The objective of the teaching packet is to illustrate to the audience the basic function of the brain, the neurobiological basis for addiction and the actions of heroin and cocaine. The packet is arranged in 4 sections. The first section introduces the brain and presents some basic neurobiology, the second introduces the reward pathway and the third and fourth present the mechanism of action of heroin and cocaine and how each affects the reward system.

Before Using the Teaching Packet

Know your target audience. Be prepared to adjust your presentation depending on the degree of education and training of your audience. Read the narrative script and practice the presentation. Be prepared to define any word used in the presentation. If you need additional information, several reference materials are also included at the end.

Additional Reference Material

G. Hanson and P.J. Venturelli. Drugs and Society, Jones and Barlett Publishers, Boston, 1995. O. Ray and C. Ksir. Drugs, Society, and Human Behavior, Mosby, St. Louis, 1996. R.R. Levine, C.A. Walsh and R.D. Schwartz. Pharmacology: Drug Actions and Reactions, Parthenon Publishing Group, New York, 1996.

- Use the narrative text as a guide, it need not be repeated word-for-word.

General Instructions

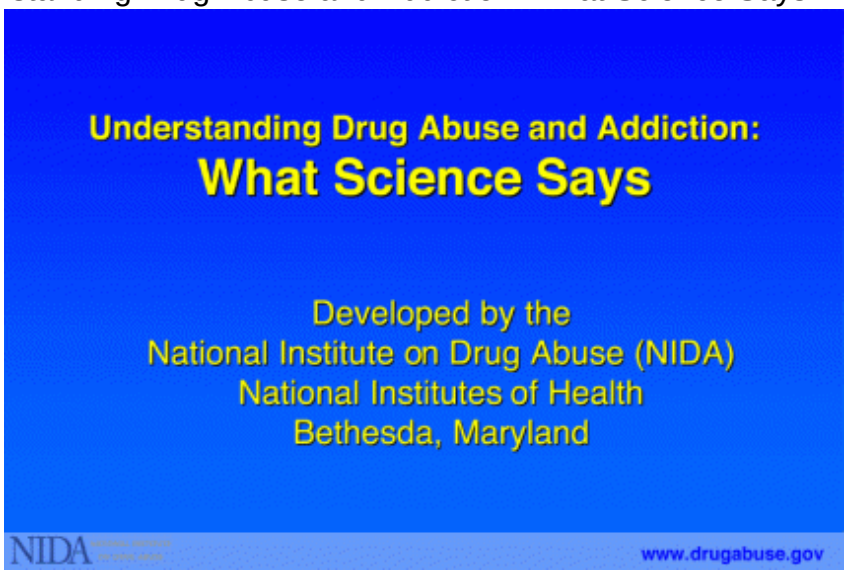
The presentation should take approximately 30-40 minutes (without questions).

Understanding Drug Abuse and Addiction: What Science Says

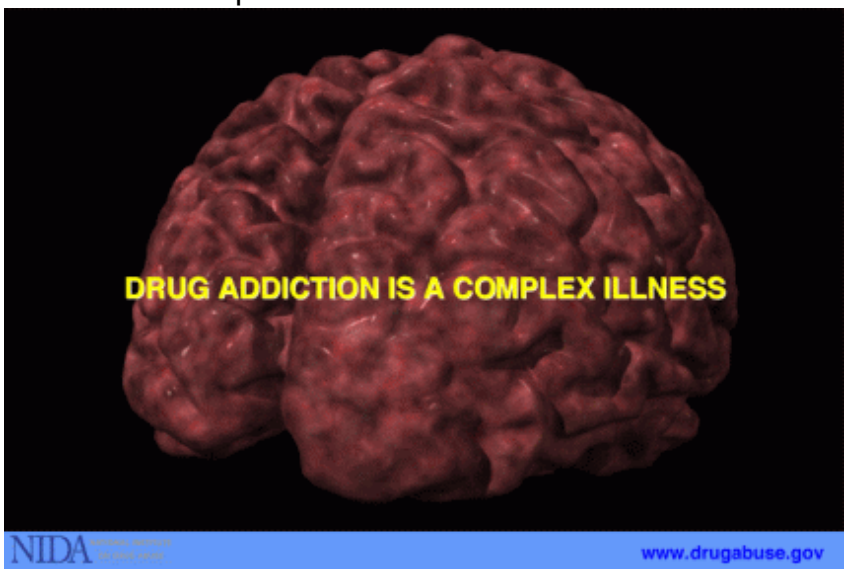
The third in a 5-part series, reviews the science behind drug abuse and addiction and introduces the topics of prevention and treatment. This presentation can be downloaded as a Powerpoint file - Understanding Drug Abuse and Addiction: What Science Says (PPT, 2MB) and was last reviewed in February, 2016

Expand All

Understanding Drug Abuse and Addiction: What Science Says

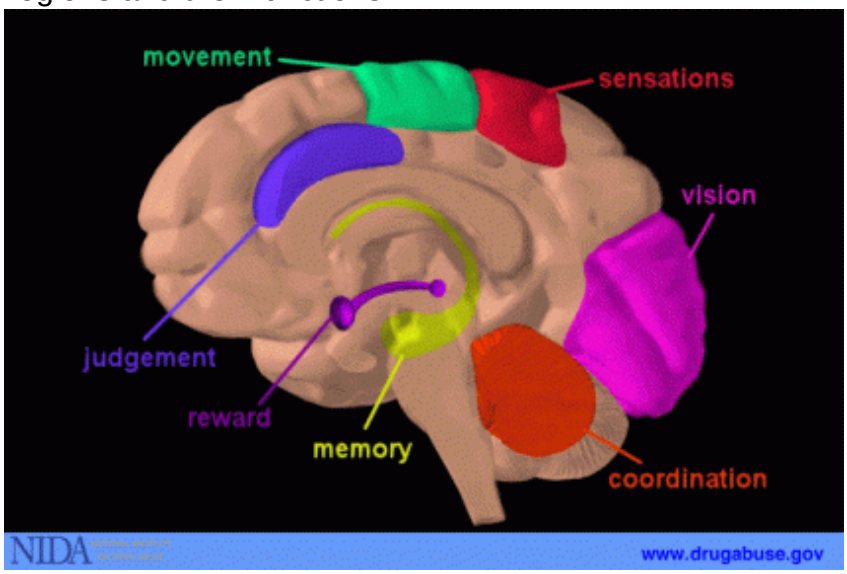


Drug addiction: a complex illness



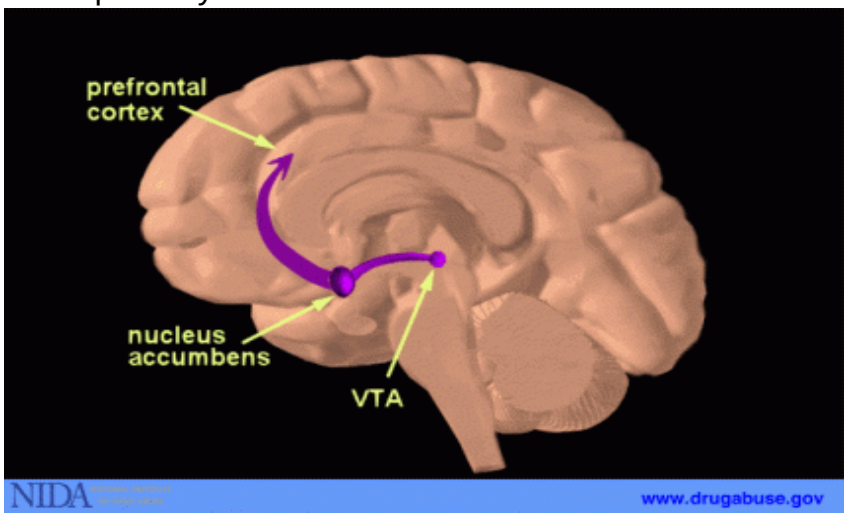
Drug addiction is a complex illness. The path to drug addiction begins with the act of taking drugs. Over time, a person's ability to choose not to take drugs is compromised. This, in large part, is a result of the effects of prolonged drug use on brain functioning, and thus on behavior. Addiction, therefore, is characterized by *compulsive drug craving, seeking, and use that persists even in the face of negative consequences*.

Brain regions and their functions



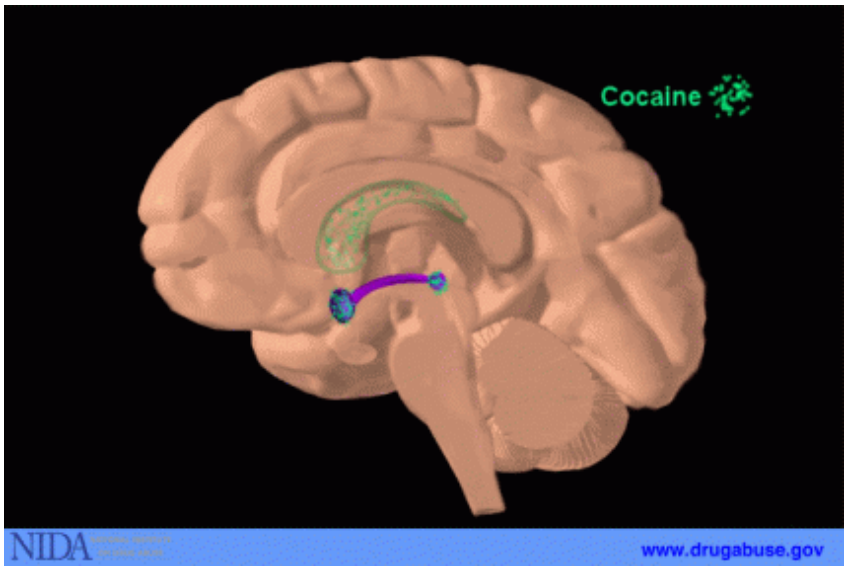
Certain parts of the brain govern specific functions. For example, the cerebellum is involved with coordination; the hippocampus with memory. Nerve cells (neurons) are the basic unit of communication in the brain. Information is relayed from one area of the brain to other areas through complex circuits of interconnected neurons. Information via electrical impulses transmitted from one neuron to many others is done through a process called "neurotransmission."

The reward pathway



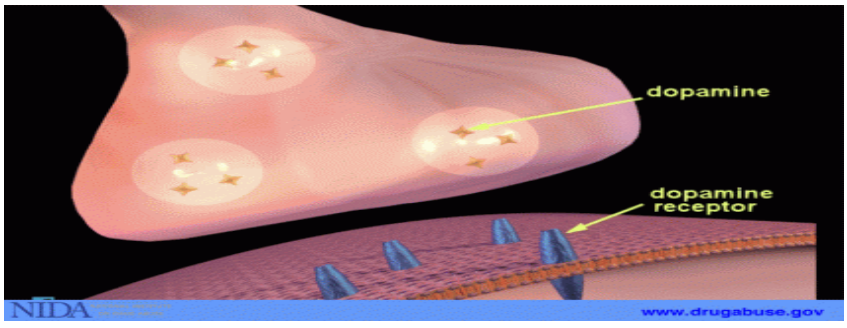
One pathway important to understanding the effects of drugs on the brain is called the reward pathway. The reward pathway involves several parts of the brain, some of which are highlighted in this image: the ventral tegmental area (VTA), the nucleus accumbens, and the prefrontal cortex. When activated by a rewarding stimulus (e.g., food, water, sex), information travels from the VTA to the nucleus accumbens and then up to the prefrontal cortex.

Where cocaine has its effects in the brain



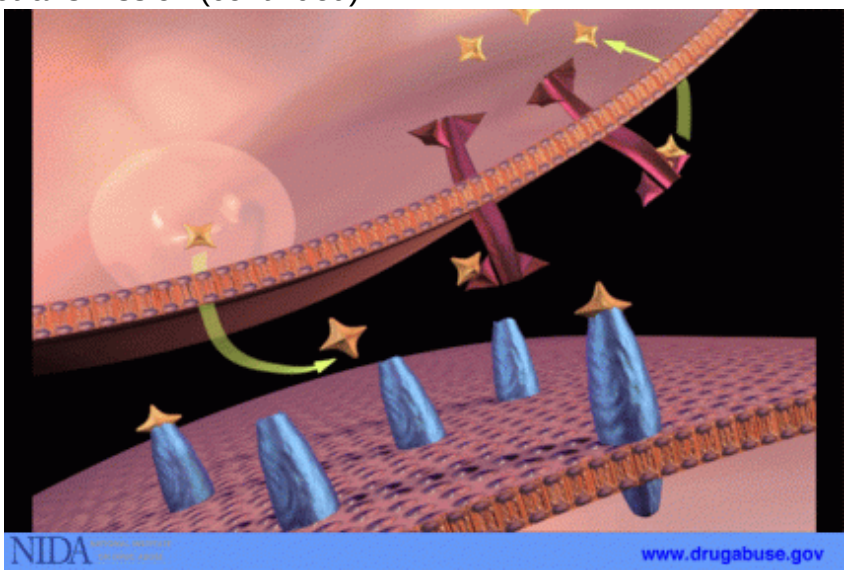
Using cocaine as an example, we can describe how drugs interfere with brain functioning. When a person snorts, smokes, or injects cocaine, it travels to the brain via the bloodstream. Although it reaches all areas of the brain, its euphoric effects are mediated in a few specific areas, especially those associated with the reward pathway discussed in the previous image.

Neurotransmission



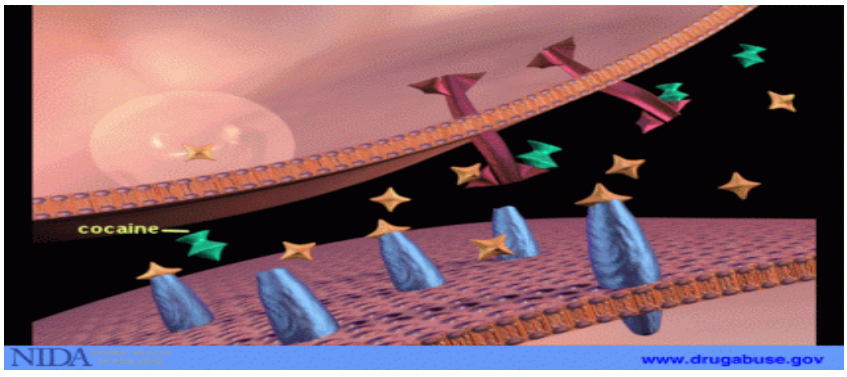
As mentioned earlier (image 3), information is communicated in the brain via a process called neurotransmission. Neurotransmission involves a variety of chemical substances called "neurotransmitters." One such neurotransmitter is called "dopamine." In the normal communication process, dopamine is released by a neuron into the synapse (the small gap between neurons). The dopamine then binds with specialized proteins called "dopamine receptors" (see image) on the neighboring neuron, thereby sending a signal to that neuron.

Neurotransmission (continued)



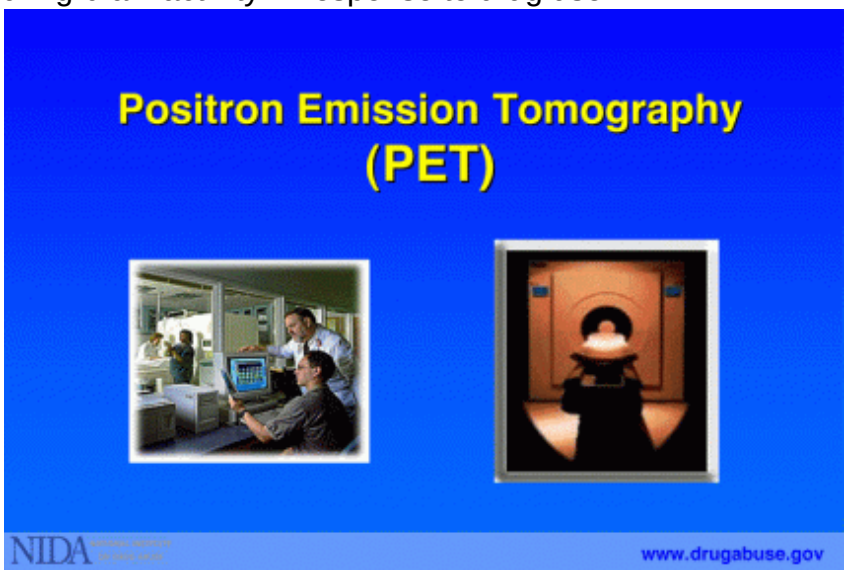
After the signal is sent to the neighboring neuron, dopamine is transported back to the neuron from which it was released by another specialized protein, the "dopamine transporter".

Cocaine and neurotransmission



Drugs of abuse are able to interfere with this normal communication process in the brain. Cocaine, for example, blocks the removal of dopamine from the synapse by binding to the dopamine transporters. As shown in this image, this results in a buildup of dopamine in the synapse. In turn, this causes a continuous stimulation of receiving neurons, probably responsible for the euphoria reported by cocaine abusers.

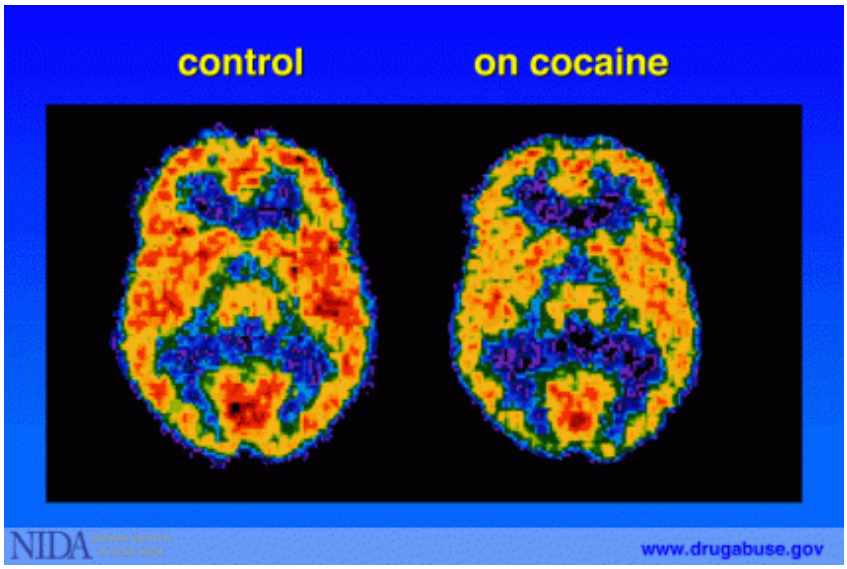
Measuring brain activity in response to drug use



Position Emission Tomography (PET) measures emissions from radioactively-labeled chemicals that have been injected into the bloodstream, and uses the data to produce images of the distribution of the chemicals in the body.

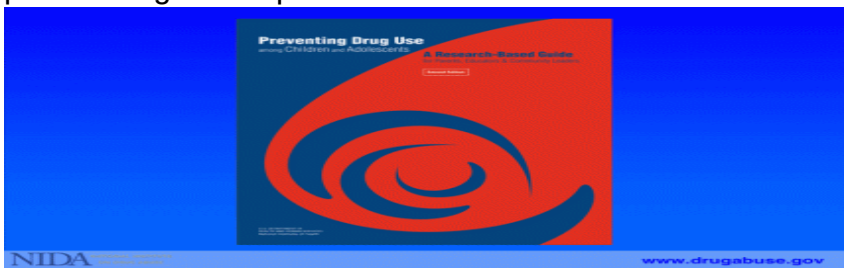
In drug abuse research, PET is being used for a variety of reasons including: to identify the brain sites where drugs and naturally occurring neurotransmitters act; to show how quickly drugs reach and activate receptors; to determine how long drugs occupy these receptors; and to find out how long they take to leave the brain. PET is also being used to show brain changes following chronic drug abuse, during withdrawal from drug use, and during the experience of drug craving. In addition, PET can be used to assess the effects of pharmacological and behavioral therapies for drug addiction on the brain.

Positron emission tomography (PET) scan of a person using cocaine



Cocaine has other actions in the brain in addition to activating the brain's reward circuitry. Using brain imaging technologies, such as PET scans, scientists can see how cocaine actually affects brain function in people. PET allows scientists to see which areas of the brain are more or less active by measuring the amount of glucose that is used by different brain regions. Glucose is the main energy source for the brain. When brain regions are more active, they will use more glucose and when they are less active they will use less. The amount of glucose that is used by the brain can be measured with PET scans. The left scan is taken from a normal, awake person. The red color shows the highest level of glucose utilization (yellow represents less utilization and blue indicated the least). The right scan is taken from someone who is on cocaine. The loss of red areas in the right scan compared to the left (normal) scan indicates that the brain is using less glucose and therefore is less active. This reduction in activity results in disruption of many brain functions.

Principles of drug abuse prevention



In 1997, NIDA published the first research-based guide on preventing drug use among children and adolescents. Using a question-and-answer format, this guide presents an overview of the research about the origins and pathways of drug abuse, the basic principles derived from effective drug abuse prevention research, and the application of these research findings. Key components of this publication are presented in the following images.

The guide is available for viewing online.

Risk and Protective Factors

Risk factors: Challenge an individual's emotional, social and academic development Protective factors: Can lessen the impact of risk factors. Their impact varies along the developmental process. Common risk factors are found for multiple adolescent problem behaviors – e.g., substance use, teen pregnancy, delinquency, school drop out, violence.

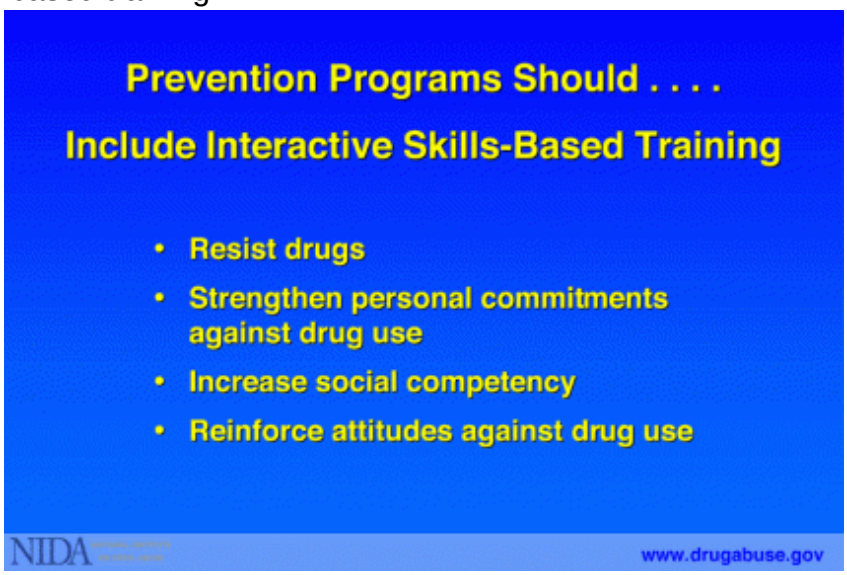
Evidence-based prevention interventions may target risk and protective factors in the individual, family, peer, school and community domains.

The Aim of Prevention Approaches is to reduce risk factors and enhance protective factors.

Targets all forms of drug use

Prevention programs should target all forms of drug use including the use of tobacco, alcohol, marijuana, and inhalants. In addition, prevention programs should be culturally sensitive to the context and needs of the individual, the family, and the community.

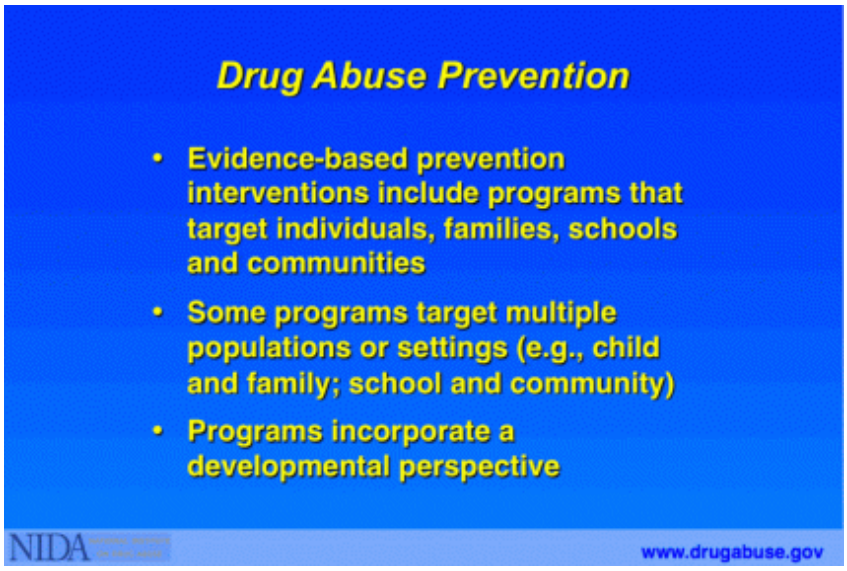
Skills-based training



Prevention programs should include skills training to help children and adolescents resist drugs, strengthen personal commitments against drug use, increase social competency (e.g.,

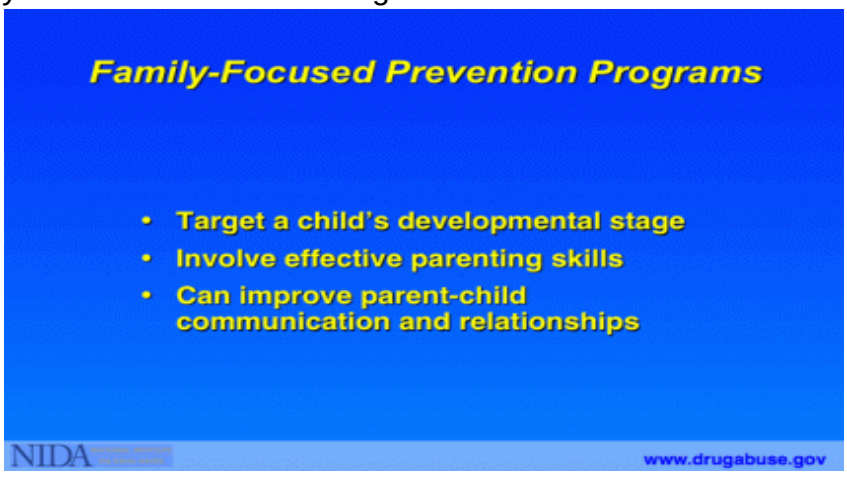
communications, peer relationships, self efficacy, and assertiveness), and reinforce attitudes against drug use. Programs should use interactive methods (e.g., group discussion) rather than didactic teaching methods alone.

Drug Abuse Prevention



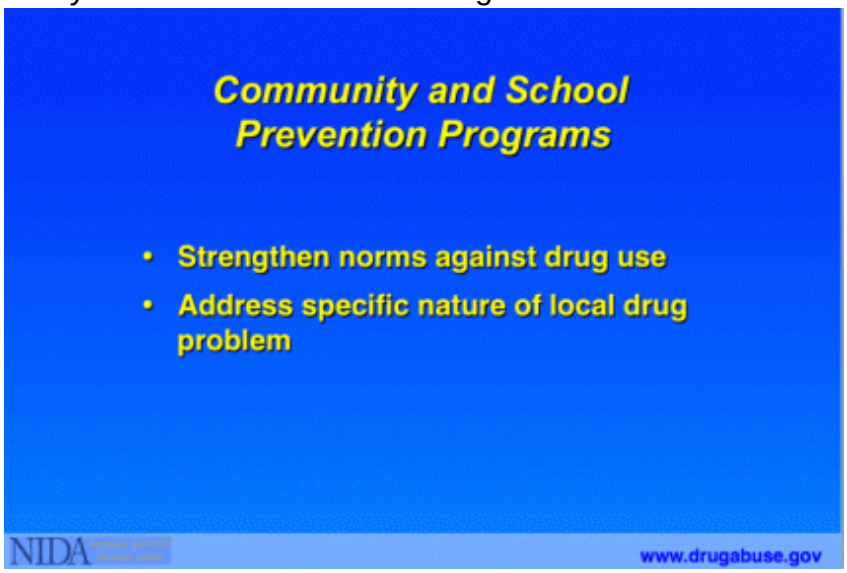
Evidence-based prevention programs target individuals, families, schools, communities, or multiple targets. Evidence-based drug abuse prevention programs often incorporate a developmental perspective.

Family-Focused Prevention Programs



Family-focused prevention programs target parents or the families, taking into consideration the stage of the child's development. Programs may provide training on effective parenting skills and monitoring to help reduce conduct problems and other risk factors for drug abuse, and improve parent-child communication and relationships.

Community and School Prevention Programs



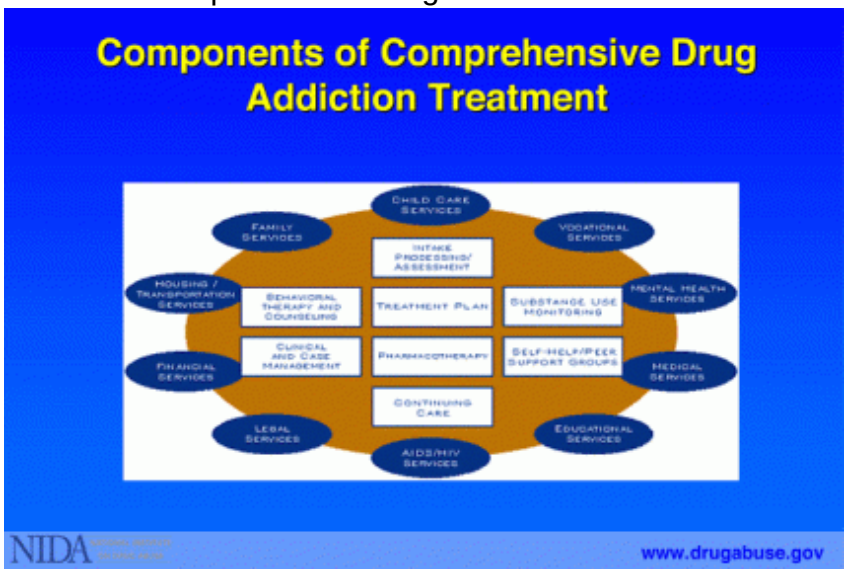
Community programs that include media campaigns and policy changes, such as new regulations that restrict access to alcohol, tobacco, or other drugs, are more effective when they are accompanied by school or family interventions. Community programs need to strengthen norms against drug use in all drug abuse prevention settings, including the family and the school. In addition, prevention programming should be adapted to address the specific nature of the drug abuse problem in the local community.

Principles of drug addiction treatment

Three decades of scientific research and clinical practice have yielded a variety of effective approaches to drug addiction treatment. In April 1998, NIDA held *The National Conference on Drug Addiction Treatment: From Research to Practice* which summarized this extensive body of research. Based on the findings reported at this conference, NIDA published in October 1999, *Principles of Drug Addiction Treatment: A Research-Based Guide* to foster more widespread use of scientifically-based components of drug addiction treatment. Key components of this guide are highlighted in the following images.

Note: The current version of this publication was revised in April 2009.

Components of comprehensive drug addiction treatment



A variety of scientifically-based approaches to drug addiction treatment exist. Drug addiction treatment can include behavioral therapy (e.g., counseling, cognitive therapy, or psychotherapy), medications, or their combination. Case management and referral to other medical, psychological, and social services are crucial components of treatment for many people as well. The best programs provide a combination of therapies and other services to meet the needs of the individual patient, which are shaped by such issues as age, race, culture, sexual orientation, gender, pregnancy, parenting, housing, and employment, as well as physical and sexual abuse.

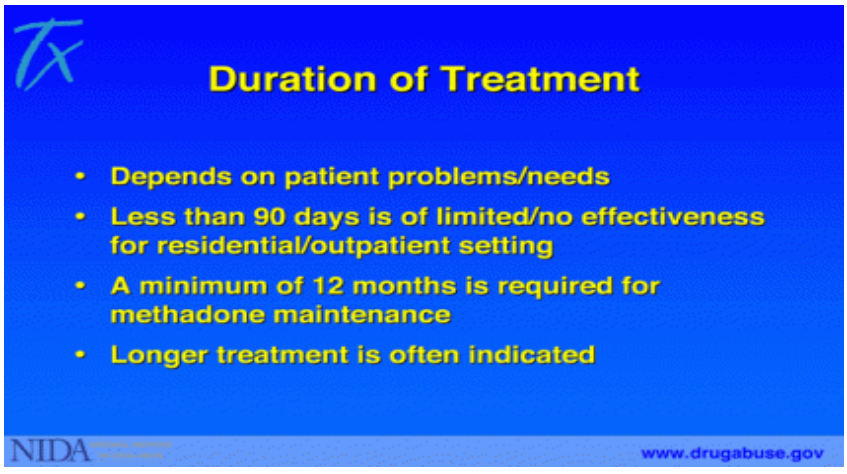
Several of the key principles underlying this approach to treatment follow.

Matching patients to individual needs

No single treatment is appropriate for all individuals. Matching treatment setting, interventions, and services to each individual's particular problems and needs is critical to his or her ultimate success in returning to productive functioning in the family, workplace, and society.

Effective treatment attends to multiple needs of the individual, not just his or her drug use. To be effective, treatment must address the individual's drug use and any associated medical, psychological, social, vocational, and legal problems.

Duration of treatment

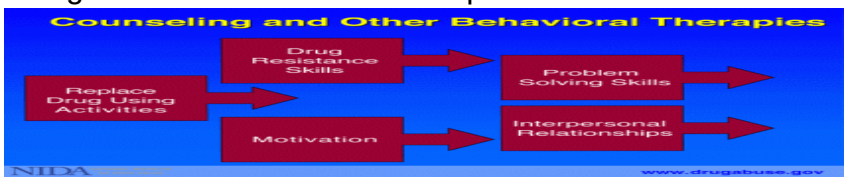


Individuals progress through drug addiction treatment at various speeds, so there is no predetermined length of treatment. However, research has shown unequivocally that good outcomes are contingent on adequate lengths of treatment. Generally, for residential or outpatient treatment, participation for less than 90 days is of limited or no effectiveness, and treatments lasting significantly longer often are indicated. For methadone maintenance, 12 months of treatment is the minimum, and some opiate-addicted individuals will continue to benefit from methadone maintenance treatment over a period of years.

Medical detoxification

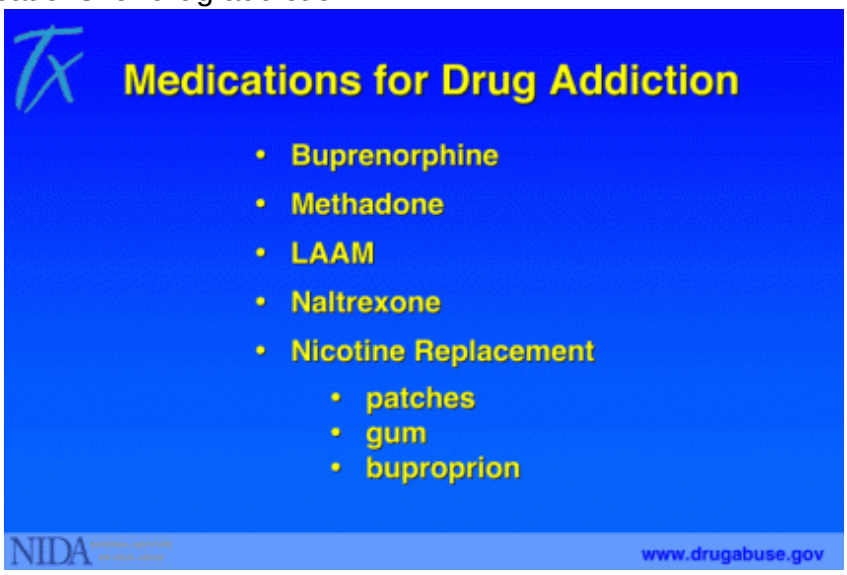
Medical detoxification safely manages the acute physical symptoms of withdrawal associated with stopping drug use. However, medical detoxification is only the first stage of addiction treatment and by itself does little to change long-term drug use. Although detoxification alone is rarely sufficient to help addicts achieve long-term abstinence, for some individuals it is a strongly indicated precursor to effective drug addiction treatment.

Counseling and other behavioral therapies



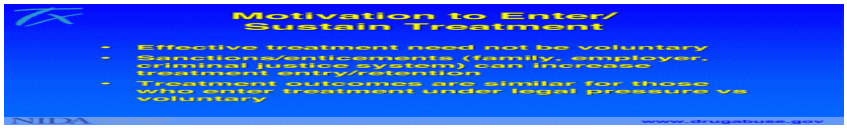
Counseling (individual and/or group) and other behavioral therapies are critical components of effective treatment for addiction. In therapy, patients address issues of motivation, build skills to resist drug use, replace drug-using activities with constructive and rewarding nondrug-using activities, and improve problem-solving abilities. Behavioral therapy also facilitates interpersonal relationships and the individual's ability to function in the family and community.

Medications for drug addiction



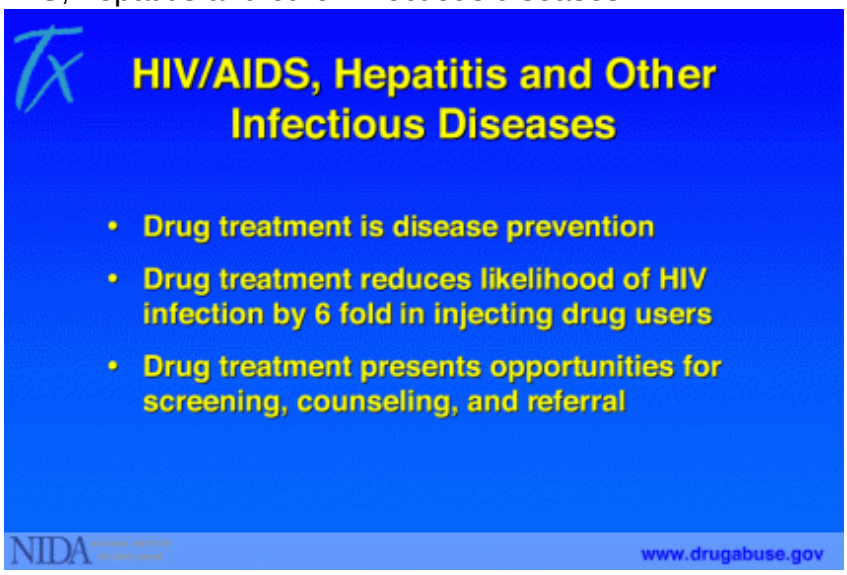
Medications are an important element of treatment for many patients, especially when combined with counseling and other behavioral therapies. Methadone and levo-alpha-acetylmethadol (LAAM) are very effective in helping individuals who are addicted to heroin or other opiates stabilize their lives and reduce their illicit drug use. Naltrexone is also an effective medication for some opiate addicts and some patients with co-occurring addiction to alcohol. For persons addicted to nicotine, a nicotine replacement product (such as patches or gum) or an oral medication (such as bupropion) can be an effective component of treatment. For patients with mental disorders, both behavioral treatments and medications can be critically important.

Motivation to enter/sustain treatment



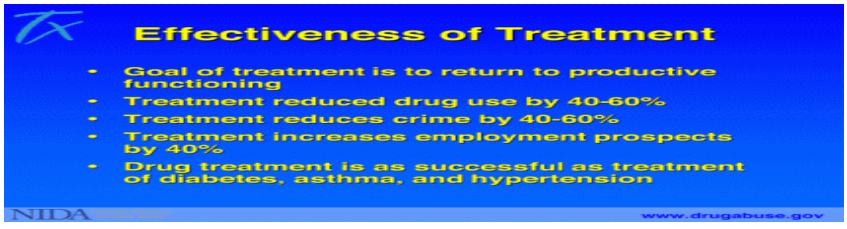
Treatment does not need to be voluntary to be effective. Strong motivation can facilitate the treatment process. Sanctions or enticements in the family, employment setting, or criminal justice system can increase significantly both treatment entry and retention rates and the success of drug treatment interventions. Individuals who enter treatment under legal pressure have outcomes as favorable as those who enter treatment voluntarily.

HIV/AIDS, hepatitis and other infectious diseases



Drug injectors who do not enter treatment are up to six times more likely to become infected with HIV than injectors who enter and remain in treatment. Drug abusers who enter and continue in treatment reduce activities that can spread disease, such as sharing injection equipment and engaging in unprotected sexual activity. Participation in treatment also presents opportunities for screening, counseling, and referral for additional services. The best drug abuse treatment programs provide HIV counseling and offer HIV testing to their patients.

Effectiveness of treatment

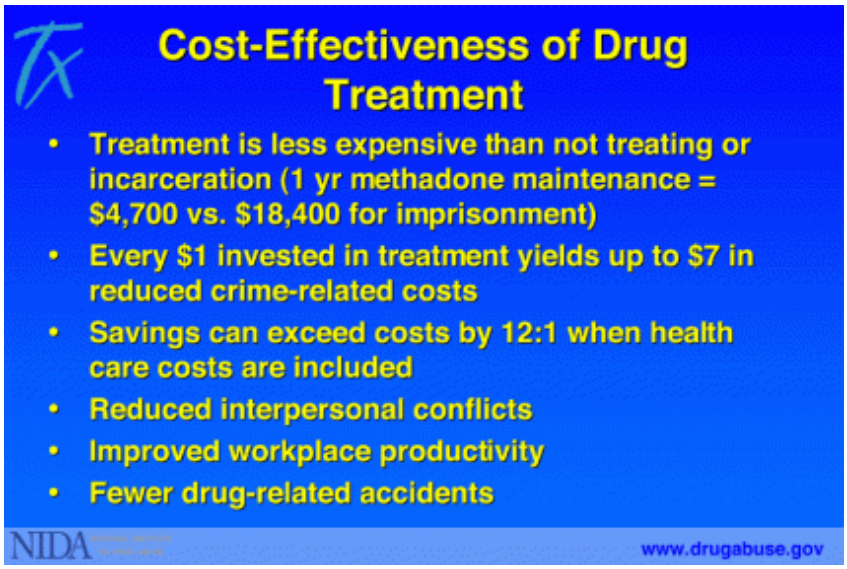


According to several studies, drug treatment reduces drug use by 40 to 60 percent and significantly decreases criminal activity during and after treatment. For example, a study of therapeutic community treatment for drug offenders demonstrated that arrests for violent and nonviolent criminal acts were reduced by 40 percent or more. Methadone treatment has been shown to decrease criminal behavior by as much as 50 percent. Research shows that drug addiction treatment reduces the risk of HIV infection and that interventions to prevent HIV are much less costly than treating HIV-related illnesses. Treatment can improve the prospects for employment, with gains of up to 40 percent after treatment. (Note: Although these effectiveness rates hold in general, individual treatment outcomes depend on the extent and nature of the patient's presenting problems, the appropriateness of the treatment components and related services used to address those problems, and the degree of active engagement of the patient in the treatment process.)

Self-help and drug addiction treatment

Self-help groups can complement and extend the effects of professional drug addiction treatment. The most prominent self-help groups are those affiliated with Alcoholics Anonymous (AA), Narcotics Anonymous (NA), and Cocaine Anonymous (CA), all of which are based on the 12-step model and Smart Recovery. Most drug addiction treatment programs encourage patients to participate in a self-help group during and after formal treatment.

Cost effectiveness of drug treatment



Drug addiction treatment is cost-effective in reducing drug use and its associated health and social costs. Treatment is less expensive than alternatives, such as not treating addicts or simply incarcerating addicts. For example, the average cost for 1 full year of methadone maintenance treatment is approximately $4,700 per patient, whereas 1 full year of imprisonment costs approximately $18,400 per person.

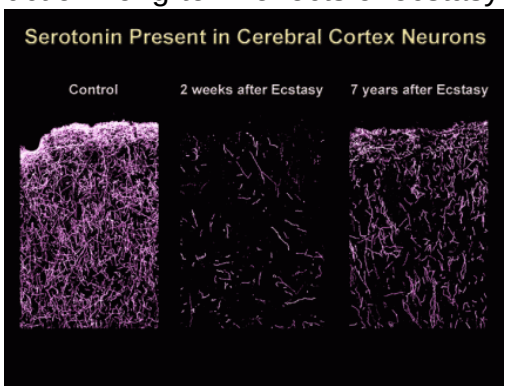
According to several conservative estimates, every $1 invested in addiction treatment programs yields a return of between $4 and $7 in reduced drug-related crime, criminal justice costs, and theft alone. When savings related to health care are included, total savings can exceed costs by a ratio of 12 to 1. Major savings to the individual and to society also come from significant drops in interpersonal conflicts, improvements in workplace productivity, and reductions in drug-related accidents.

The Neurobiology of Ecstasy (MDMA)

The fourth in a 5-part series, explores the biology behind ecstasy use in the brain and discusses both short- and long-term effects of its use. This presentation can be downloaded as a Powerpoint file - The Neurobiology of Ecstasy (PPT, 7MB) and was last reviewed in January, 2007

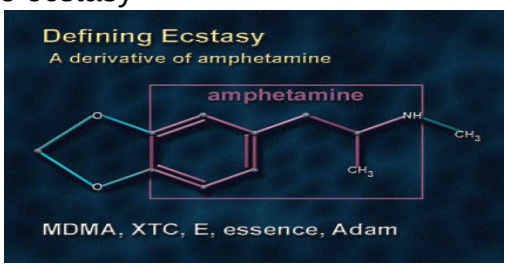
Expand All

Introduction: long-term effects of ecstasy



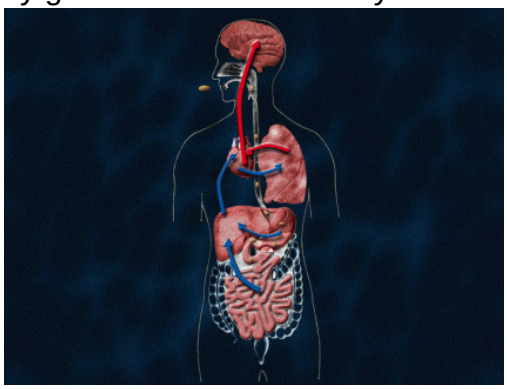
An effective way of starting a presentation is to present something interesting or provocative. This first image shows sections taken from the neocortex of monkeys that were given ecstasy twice a day for 4 days (control monkeys were given saline). The section on the left, taken from the brain of a control monkey, shows the presence of a lot of serotonin. The middle section shows a section from a monkey two weeks after receiving ecstasy. Point out that most of the serotonin is gone. The section on the right shows a section from a monkey seven years after receiving ecstasy. Point out that although there has been some recovery of serotonin, the brain still has not returned to normal. Indicate that you will discuss this in your talk in more detail. Introduce the purpose of your presentation. Indicate that you will explain how ecstasy interacts with specific targets in the brain and what can happen after repeated or long-term use. Tell the students that you will review how neurons communicate with each other and how ecstasy alters this communication, resulting in changes in mood, behavior, and memory.

Define ecstasy



Ecstasy is a derivative of amphetamine (shown in purple on the image). Its chemical name is 3,4-methylenedioxymethamphetamine (MDMA) and it has a similar structure to methamphetamine. ecstasy has a variety of street names including, XTC, Adam, M & M, E, and essence. Explain to students that ecstasy is unlike other drugs of abuse, which are often derived from plants (e.g., cocaine, morphine, nicotine). In contrast, ecstasy is synthesized in clandestine laboratories--in fact, there are several "designer drugs" that are made (in clandestine laboratories) by altering the structure of the amphetamine molecule. Because ecstasy is synthesized in laboratories, its purity can vary substantially from lab to lab, and other compounds are easily combined into the same tablet (contaminants often include caffeine, ephedrine, ketamine - a mild hallucinogen and methamphetamine).

Ecstasy gets into the brain easily



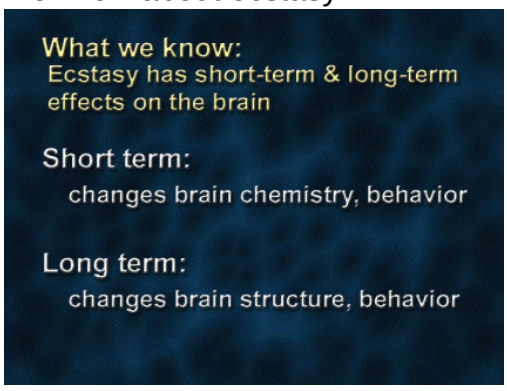
The chemical structure of ecstasy allows it to reach the brain quickly after ingestion. Use the image to illustrate to the students the pathway that ecstasy follows from the mouth to the brain. First, the pill is ingested and it disintegrates quickly in the stomach contents. Once dissolved, some ecstasy molecules are absorbed from the stomach into the bloodstream, but most of the ecstasy molecules move from the stomach into the small intestine. There, they are absorbed into the bloodstream very easily.

The following explanation is optional and may be desirable for presentation to students who have had some chemistry: ecstasy is a weak base--this means that ecstasy is likely to "pick up" or accept a hydrogen ion (H+) from the surrounding medium (the gastric acid in the stomach is

loaded with H+). After the ecstasy has accepted a H+, it has a charged (or polar) character, which makes it difficult to cross a biological membrane. Biological membranes have a nonpolar core, so compounds having a nonpolar nature are more likely to diffuse across the membrane (passive diffusion). Therefore, most of the ecstasy is not absorbed from the stomach into the bloodstream. Rather, the ecstasy molecules get emptied from the stomach into the small intestine. In the small intestine the more alkaline environment causes ecstasy to give up its H+, becoming more nonpolar. The large surface area and the more alkaline environment enable the ecstasy molecules to diffuse across the membrane into the blood capillaries very quickly.

Ecstasy molecules that have entered the bloodstream from the stomach and small intestines then travel to the liver (shown by the bottom blue arrows). In the liver, some of the ecstasy is metabolized to inactive compounds and the rest is carried through the veins to the heart (blue arrow). Once in the heart, the ecstasy is pumped to the lungs along with the blood, which becomes oxygenated and then returns to the heart (red arrow). Now, oxygenated blood carries the ecstasy from the heart to the brain (red arrow) and to other organs in body that have a high blood flow. Normally there is a barrier between the blood vessels in the brain and brain matter, which excludes many drugs from entering the brain. However, ecstasy is predominantly in its nonpolar form in blood and therefore it crosses the barrier into the brain very easily. It will take about 15 minutes for ecstasy to reach the brain if taken on an empty stomach.

What we know about ecstasy



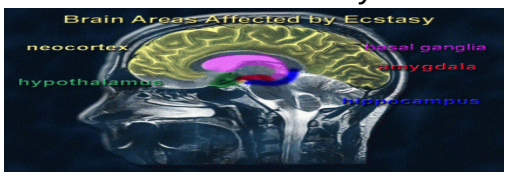
In recent years, there has been a lot of research carried out to understand how ecstasy affects the brain. Scientists have made a lot of progress in identifying how ecstasy changes mood and

behavior. Indicate to students that ecstasy has short-term and long-term effects on the brain. The short-term effects of ecstasy include changes in brain chemistry and behavior. The long-term effects include changes in brain structure (based mainly on animal studies) and behavior. Tell them that you will try to illustrate how these changes take place. You could ask students if they have any knowledge of the short-term or long-term effects of ecstasy on the brain. If they volunteer some answers, list them on the board; indicate that you will discuss how some of these effects are produced.

How do we know? Research in animals and humans

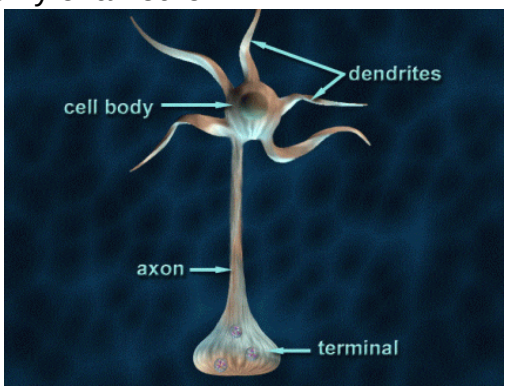
Bring up the importance of animals in research. Research in animals has provided us with a detailed understanding about the actions of ecstasy in the brain. In fact, many of the research findings obtained from animals, such as rats and monkeys, have now been replicated in humans. Indicate to the students that another important aspect of using animals in research is to understand mechanisms for toxicity produced by compounds. ecstasy is a classic example of a drug that produces toxicity (in the brain) and it would be impossible to study this in living humans. In the following set of images, the information highlighting how ecstasy works was obtained from research using animals.

Brain areas sensitive to ecstasy



Before explaining how ecstasy works, it may be helpful to point out the areas of the brain that are sensitive to the effects of ecstasy. ecstasy affects cognition (thinking), mood, and memory. It also can cause anxiety and altered perceptions (similar to but not quite the same as hallucinations). The most desirable effect of ecstasy is its ability to provide feelings of warmth and empathy. Tell students that you will talk about the effects of ecstasy in more detail in a few minutes. There are several parts of the brain that are important in these actions of ecstasy. Point to the neocortex (in yellow), which is important in cognition, memory, and altered perceptions. Point to the several structures deep in the brain that make up the limbic system (e.g., the amygdala (red), hippocampus (blue), basal ganglia (purple), and hypothalamus (green), which is involved in changes in mood, emotions, and the production of anxiety (the hippocampus is also involved in memory). Scientists do not know yet which area of the brain is involved in the ability of ecstasy to generate feelings of empathy (you could ask students to suggest where they think ecstasy might do this - limbic areas are a good guess).

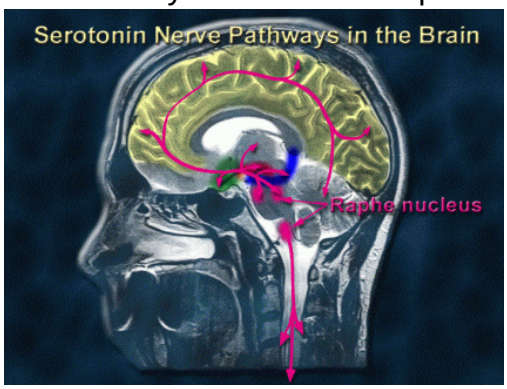
Anatomy of a neuron



Now that the students know that there are specific regions of the brain affected by ecstasy, you will need to describe how it works. First, indicate that the different regions of the brain are connected by nerve cells or neurons via pathways. These pathways of neurons send and integrate information (electrical and chemical). Describe the neuron using the schematic in this image. The cell body, which contains the nucleus, is the center of activity. Dendrites receive chemical information from other neurons that is converted to electrical signals which travel toward the cell body. When the cell body receives enough electrical signals to excite it, a large electrical impulse is generated and it travels down the axon toward the terminal. In the terminal

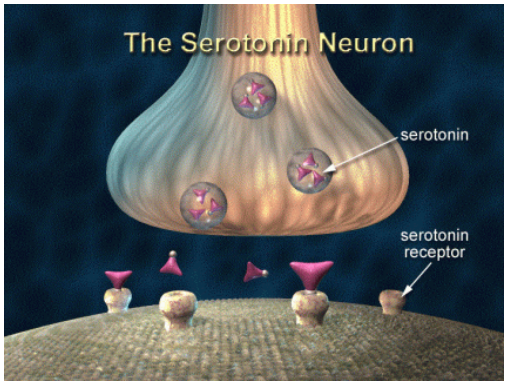
area, chemicals called neurotransmitters are released from the neuron in response to the arrival of an electrical signal. Tell the students that you will explain this in more detail, using the neurochemical serotonin as an example.

How does ecstasy work: serotonin pathways in the brain



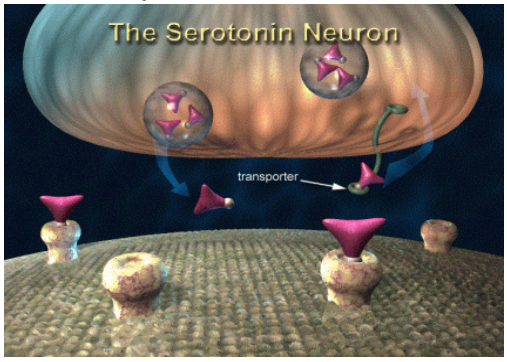
The nerve pathway that is predominantly affected by ecstasy is called the serotonin pathway. Serotonin is a neurotransmitter that is synthesized, stored, and released by specific neurons in this pathway. It is involved in the regulation of several processes within the brain, including mood, emotions, aggression, sleep, appetite, anxiety, memory, and perceptions. Tell the students that you will show them how a chemical like serotonin can regulate these processes. First, describe how serotonin pathways innervate (connect to) different brain regions. Point to the cell bodies of the serotonin pathway that are located in the brainstem area "the Raphe nucleus" in pink). Show students how these neurons send long axons to higher centers in the brain including the neocortex (yellow) and the limbic system (e.g., the amygdala--red and hippocampus--blue). Point to a second pathway for serotonin neurons that descends down the spinal cord; these neurons control muscle activity; tell the students that you will talk about this in more detail in a few minutes. Indicate that the function of serotonin depends on the region of the brain into which it is released (it also depends on the type of serotonin receptor present in that region--see discussion in image 9). For example, the serotonin neurons in the neocortex in the front of the brain (frontal cortex) regulate cognition, memory, and perceptions. The serotonin neurons in the hippocampus regulate memory. The serotonin neurons in other limbic areas such as the amygdala also regulate mood.

The serotonin neuron: the major target of ecstasy



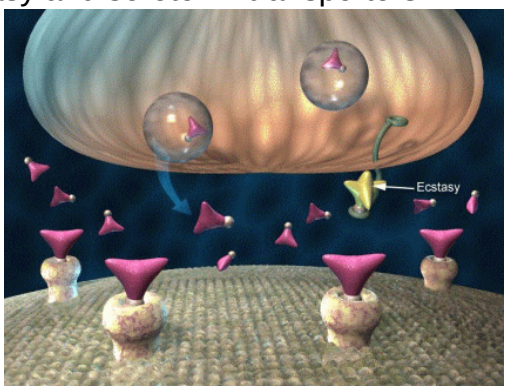
In order to help students understand how ecstasy affects the function of serotonin neurons, it will be useful to review how neurotransmission takes place in a little more detail. You can explain serotonin neurotransmission as an example (serotonin is one of many neurotransmitters). This image shows the connection between two neurons (the "synapse"). Serotonin is stored in small vesicles within the nerve terminal of a neuron. Electrical impulses (arising in the Raphe nucleus, for example) traveling down the axon toward the terminal cause the release of serotonin from small vesicles into the synaptic space. Point to the space between the terminal and the neighboring neuron. When in the synaptic space, the serotonin binds to special proteins, called receptors, on the membrane of a neighboring neuron (this is usually at a dendrite or cell body). When serotonin binds to serotonin receptors (there are actually at least 14 types of serotonin receptors), it causes a change in the electrical properties of the receiving neuron that generally results in a decrease in its firing rate. Go to the next image to explain how the action of serotonin is terminated.

Serotonin transporters



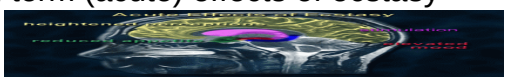
Serotonin (in pink) is present in the synaptic space only for a limited amount of time. If it is not bound to the serotonin receptor, serotonin is removed from the synaptic space via special proteins called transporters (in green). The serotonin transporters are proteins located on the serotonin neuron terminals and they are in a unique position to transport serotonin from the synaptic space back into the neuron where it can be metabolized by enzymes. Explain to your students that the serotonin transporters are the primary targets for ecstasy.

Ecstasy and serotonin transporters



When ecstasy binds to the serotonin transporters, more serotonin ends up in the synaptic space. This occurs for two reasons. First, ecstasy can prevent the transporters from carrying serotonin back into the terminal. Second, ecstasy can cause the transporters to work in reverse mode--they actually bring serotonin from the terminal into the synaptic space. So, more serotonin is present in the synaptic space and more serotonin receptors become activated. This is the major short-term effect of ecstasy that alters brain chemistry. Although the serotonin system is the primary target for ecstasy, ecstasy has similar effects on the dopamine (another neurotransmitter) system as well. ecstasy can inhibit dopamine transporters and cause an increase in dopamine levels in the synaptic space (not shown here). To help students understand how the alteration in brain chemistry results in psychological changes, go to the next image.

Short-term (acute) effects of ecstasy

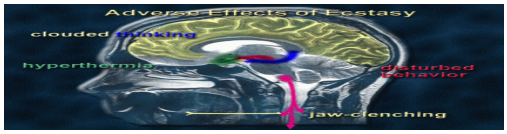


Explain that when a person uses ecstasy, the increase in serotonin in different brain regions (i.e., the areas where serotonin neurons traveling from the raphe nucleus terminate) causes psychological effects. These include elevated mood and feelings of empathy. The ecstasy is also reinforcing, which means that its pleasurable properties increase the likelihood that the person will take it again. Tell the students that drugs that are reinforcing are usually addictive.

Students might ask you if ecstasy is addictive. Scientists and health professionals don't have a definitive answer yet. For now there are several pieces of evidence that suggest that ecstasy has the potential to be addictive. In one study of ecstasy users, 43% of respondents met criteria that are commonly used to determine dependence for other drugs of abuse. This included symptoms such as continuing to use the drug despite knowledge of physical or psychological harm, experiencing withdrawal effects, and tolerance (or diminished response) to repeated use of ecstasy. In a research setting, monkeys will administer ecstasy to themselves (they actually press a lever to obtain an injection), just as they do for other addictive drugs. Monkeys will not self-administer drugs that are not addictive. In addition, there is emerging research to show that ecstasy has actions in a specific pathway within the limbic system called the "reward pathway", which can explain it's reinforcing effects. In fact, all addictive drugs act in some way within the "reward pathway". For more information on this, see the NIDA Teaching Packet referenced at the end.

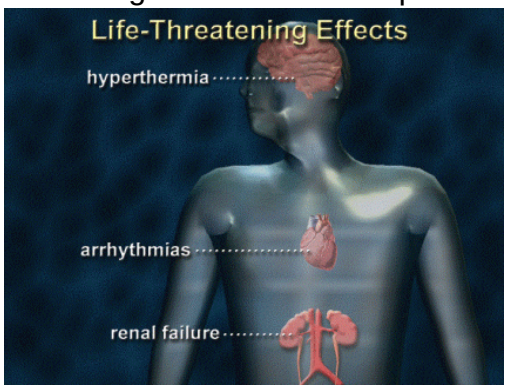
Many of the psychological effects of ecstasy are due to its actions within the limbic system (the amygdala, in red, and hippocampus, in blue, especially). The ability of ecstasy to produce mild stimulation is due to its actions in another part of the limbic system -- the basal ganglia (in purple). It is here where ecstasy's effects on the dopamine system may be important. The heightened perceptions involve the actions of ecstasy in the neocortex (in yellow). ecstasy can also reduce the appetite, because it acts in the hypothalamus (in green), which controls feeding behavior.

Short-term adverse effects



People who take ecstasy desire its pleasurable or reinforcing effects (just described in the last image). However, few drugs are able to produce desirable effects without also producing side effects. ecstasy is no exception, and there are several side effects or adverse effects that can occur, especially at high doses. However, some people who take only one ecstasy pill may have negative psychological effects such as clouded thinking, agitation, and disturbed behavior. Point to areas of the brain where ecstasy may produce these adverse effects (the neocortex, in yellow and limbic structures, in red and blue). Other adverse effects can occur as well. These include sweating, dry mouth (thirsty), increased heart rate, fatigue, muscle spasms (especially jaw-clenching) and hyperthermia. In the latter case, ecstasy can disrupt the ability of the brain to regulate body temperature. This usually results in hyperthermia, especially when the user is in a hot environment and/or engaging in intense physical activity such as fast dancing at "rave" parties. You can provide some examples to show where ecstasy produces these side effects. For example, the development of thirst and the hyperthermia are due to actions of ecstasy in the hypothalamus (green), which controls drinking behavior and body temperature. You might point out that the effect of ecstasy on the hypothalamus causes multiple effects in the body, and in some cases they are very dangerous (see the next image). The muscle spasms and jaw-clenching are due to ecstasy's action at the motor neurons in the spinal cord (in yellow) (remind the students that a major serotonin pathway descends down the spinal cord). The motor neurons send signals to the muscles to contract.

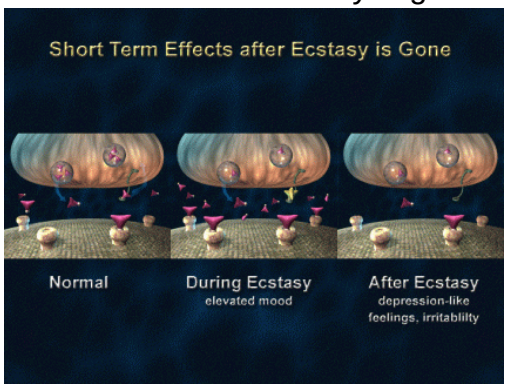
Life-threatening effects after multiple doses or *stacking*



Some people take multiple doses of ecstasy in one night ("stacking"). This might be due to the reinforcing effect of the drug wearing off over time. Often, if something feels good, one wants to

do it again! Unfortunately, increased doses also increase the adverse effects, and some of these can become life-threatening. For example, repeated doses or a high dose of ecstasy can cause heat injury due to hyperthermia, hypertension (high blood pressure), cardiac arrhythmias (irregular heart beat), muscle breakdown and renal failure due to salt and fluid depletion. Indicate that these dangerous effects can be produced by ecstasy acting in the brain. Again, the hypothalamus is very important, because it regulates heart rate and blood pressure, fluid retention and kidney function and, of course, body temperature. If the body temperature gets too high, it can cause brain damage or even kill a person.

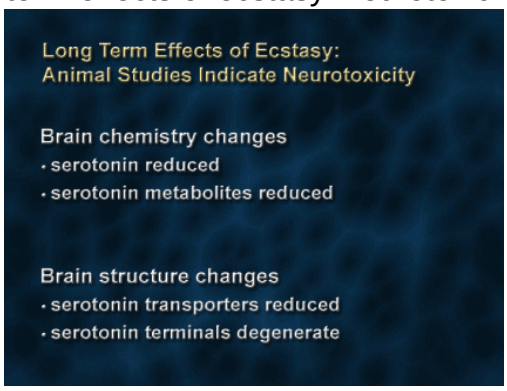
Short-term effects after ecstasy is gone from the body



Ecstasy is an unusual drug because it has effects on the brain that develop and persist for a short time after the drug is eliminated from the body. These often include the development of depression-like feelings, anxiety, restlessness, irritability, and sleep disturbances. These "after effects" occur because of a chemical change that takes place at the serotonin synapse. To illustrate how this occurs, this image shows the serotonin synapse during and after taking ecstasy. Three conditions are illustrated: on the left, neurons normally release serotonin in response to electrical impulses (basically the release is in "spurts"). This results in the normal activation of serotonin receptors, which keeps our psychological and physiological function on an even keel. So, for example, we have a normal mood and we are calm. In the middle, ecstasy causes a sustained increase in the amount of serotonin in the synaptic space, leading to sustained activation of more serotonin receptors. This can produce an elevated mood (or euphoria). Eventually, the serotonin neurons can't make serotonin fast enough to replace that which was lost, so once Ecstasy is gone from the body (on the right), less serotonin is released

with each electrical impulse and fewer serotonin receptors are activated, producing depression-like feelings and anxiety. Another important effect that may emerge after taking ecstasy is memory disruption. (Ask students if they can figure out which area of the brain is affected here; the answer should include the cerebral cortex and the hippocampus). This is an adverse effect that may persist with repeated or long-term use of ecstasy. Indicate to students that there is some evidence for this obtained from human studies.

Long-term effects of ecstasy: neurotoxic?



When people use Ecstasy repeatedly or long term, there may be changes in their brain chemistry that suggest that the serotonin neurons are damaged. One major clue is that serotonin itself and its metabolites (remind students that serotonin that is taken back up into the terminal is metabolized by enzymes) are diminished in the brains of animals treated with ecstasy. Moreover, the best evidence that we have so far is that even seven years after a brief exposure to ecstasy, serotonin levels in monkey brains have not fully returned to normal. This is described in the next image.

Long-term effects in monkeys

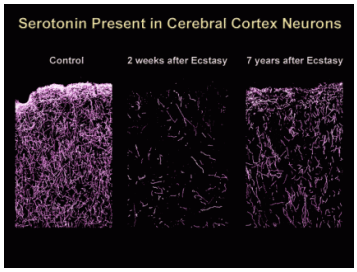


Image courtesy of Dr. GA Ricaurte, Johns Hopkins University School of Medicine.

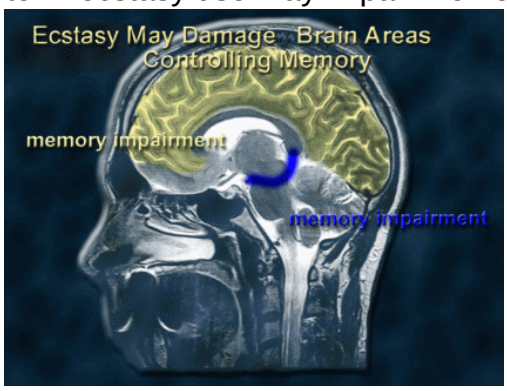
A very important experiment was performed in monkeys to determine if ecstasy can actually damage neurons. Monkeys were given ecstasy twice a day for four days (control monkeys were given saline). One group of monkeys' brains were removed two weeks later for analysis and another group of monkeys lived for an additional seven years before their brains were removed. Scientists examined the brains for the presence of serotonin. This image shows the presence of serotonin in neurons of the neocortex from three typical monkeys. On the left, the monkey who did not receive any ecstasy had a lot of serotonin (in pink) in the neocortex. Two weeks after a monkey received ecstasy, most of the serotonin was gone (point to the middle panel), suggesting that the serotonin neuron terminals were destroyed (there was no destruction of the serotonin cell bodies arising back in the brainstem). Point to the right-hand panel and show students that this damage appeared to be long-term because seven years later there was some recovery, but it was not complete. Scientists found similar changes in limbic areas of the brain such as the hippocampus and amygdala. The monkey experiments are an important reminder that humans may suffer the same fate, although this still remains to be demonstrated. Tell the students how difficult it is to do this same kind of experiment in humans, because it requires removing pieces of the brain to look for the loss of the serotonin neurons.

Ecstasy causes degeneration of serotonin nerve terminals

This image illustrates the degeneration of serotonin nerve terminals after long-term or repeated use of ecstasy (you can refer back to image 9 to compare this degenerating terminal to a healthy terminal). Remind students that we have several pieces of evidence that support this effect of ecstasy. Experiments in animals given ecstasy indicate that this kind of degeneration occurs. Moreover, some studies of human ecstasy users report less serotonin and serotonin metabolites in the cerebrospinal fluid (which surrounds and bathes the brain and spinal cord) compared with nonusers. In contrast, the animal studies indicate that the serotonin cell bodies are still intact but the genetic instructions from the nucleus for any regrowth of the terminals may be abnormal.

Although scientists do not yet know for certain how ecstasy damages the serotonin terminals in these animal studies, some progress has been made in understanding this process. One mechanism is damage that involves the production of oxygen radicals (unstable forms of oxygen), which are very destructive to proteins, lipids, and DNA. The rich supply of mitochondria (which are a major source of oxygen radical formation) found in the terminals may cause the terminals to be especially sensitive to drugs like ecstasy.

Long-term ecstasy use may impair memory



It is not possible to look directly at damaged serotonin terminals in living humans. The best evidence for damage to serotonin neurons after long-term or repeated Ecstasy use in humans is the association between the neurochemical and behavioral changes. Although many behavioral measures have been assessed in Ecstasy users (the list is extensive), the most consistent findings are that some chronic Ecstasy users have verbal and visual memory impairments. Research is ongoing to determine if thinking ability is disrupted as well. However, it is important

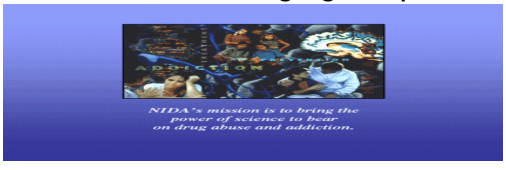
to keep in mind that many users of Ecstasy may unknowingly be taking other drugs that are sold as Ecstasy, and/or they may intentionally use other drugs, such as marijuana, which may contribute to the observed deficits in memory. Additionally, most studies in people do not have measures of memory ability in Ecstasy users before they began taking drugs. Therefore, it is difficult to rule out pre-existing memory deficits in Ecstasy users compared to nonusers. Nevertheless, in some studies Ecstasy users who had memory impairments also had less serotonin metabolites or changes in other markers of serotonin function. In fact, several studies have shown that the degree of impairment or the changes in markers of serotonin function were related to the extent of Ecstasy use over the lifetime. On the image, point to the brain areas that are involved in the memory impairment - the neocortex (yellow) and the hippocampus (blue). [As an aside, you can tell students an interesting link between low serotonin and memory impairment: normal people who are fed a diet that causes them to synthesize less serotonin also have memory impairment.]

Bringing the Power of Science to Bear on Drug Abuse and Addiction

The fifth in a 5-part series, summarizes the science behind drug abuse and addiction, reviews the harmful consequences of drug use, and poses the question of whether it is worth the risk. This presentation can be downloaded as a Powerpoint file - Bringing the Power of Science to Bear on Drug Abuse and Addiction (PPT, 1.3MB) and was last reviewed in January, 2007.

Expand All

NIDA is dedicated to bringing the power of science to bear on drug abuse and addiction



The National Institute on Drug Abuse (NIDA) is part of the National Institutes of Health and is dedicated to bringing the power of science to bear on drug abuse and addiction.

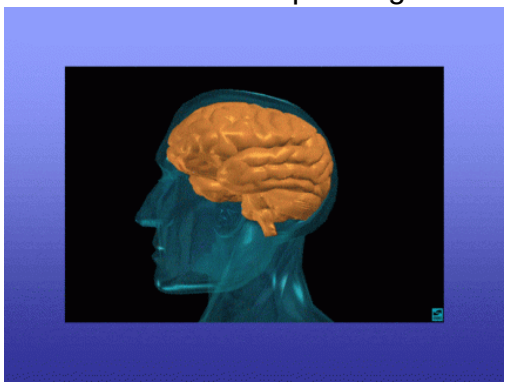
When a person first thinks about trying drugs, it is usually a voluntary decision. “Maybe I should see what it’s like... just this once,” you might think. Or a friend dares you. Or you just want to feel good or forget your troubles. Most drugs of abuse - including nicotine, alcohol, marijuana, cocaine, and heroin - activate a part of the brain called the *reward system*, and that makes you feel good. But just for a little while.

Drug abuse has serious consequences. The most serious consequence is that prolonged drug use can *change the brain* in fundamental and long-lasting ways. Eventually, it becomes difficult to deerive pleasure from other normal activities, such as sports, food, or sex.

After repeated drug use, you reach a point when deciding to use drugs is no longer voluntary. Scientists have proof now that drugs literally *change* your brain. It’s as if a “switch” goes off in the brain. It is during this transformation process that a *drug abuser* becomes a *drug addict*.

Addiction is a chronic relapsing disease characterized by compulsive, often uncontrollable, drug seeking and drug use in the face of negative consequences. Drug addicts need professional help and treatment to help them cope with these changes and *possibly* change the brain back to normal.

The brain is the most complex organ in the body



The brain is made up of a complex network of billions of nerve cells called *neurons*, as well as other kinds of cells, all protected by the bones of the skull. The typical brain weighs only about 3 pounds, but it is the source of most qualities that make you who you are. Neurons in the brain and spinal cord are part of the nervous system and act as a body's "Command Central."

The brain is constantly active, even when we are asleep. As a matter of fact, asleep or awake, the brain requires 20 percent of the heart's output of fresh blood and 20 percent of the blood's oxygen and glucose to keep functioning properly. Glucose is a type of sugar that is our brain's primary fuel.

The brain produces enough electrical energy to power a 40-watt light bulb for 24 hours. That's a lot of energy for a human organ a little bigger than a softball.

How a neuron works

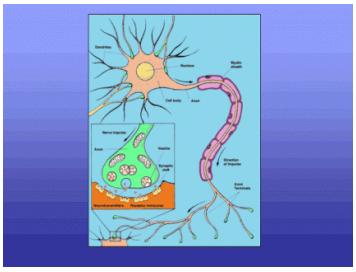


Illustration used with permission, courtesy of Lydia V. Kibiuk and the Society for Neuroscience

Neurons are unique because they can send information from the brain to the rest of the body. Your brain communicates with the rest of your body by sending messages from one neuron to the next and ultimately to the muscles and organs of the body. Neurons can also store information as memories.

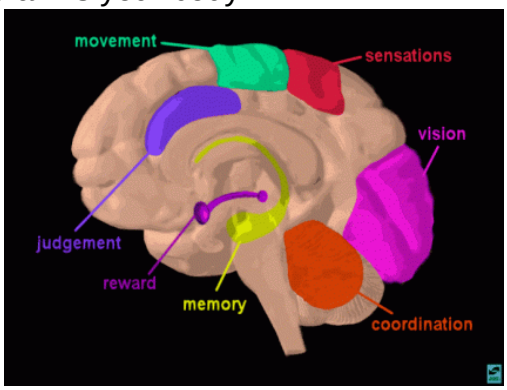
Typically, a neuron contains three important parts: a *cell body* that directs all activities of the neuron; *dendrites* (the part that looks like tree branches), which are short fibers that receive messages from other neurons and relay those messages to the cell body; and the *axon*, a long

single fiber that transmits messages from the cell body to dendrites of other neurons. Every moment, messages are moving with amazing speed back and forth from neuron to neuron. As a matter of fact, scientists often compare the activity of neurons to the way electricity works.

A neuron communicates with other neurons at special places called *synapses* or *synaptic clefts*. To send a message, a neuron releases a chemical messenger, or *neurotransmitter*, into the synaptic cleft. From there, the *neurotransmitter* crosses the synapse and attaches to key sites called receptors on the next neuron in line. When neurotransmitters attach to these receptors, they cause changes inside the receiving neuron and the message is delivered.

Neurons communicate with each other through a network of interconnected cells that scientists are still trying to fully understand. Scientists *do* know that this complex communication system within the brain can be disrupted by the chemicals in drugs. Did you know that more than 400 chemicals are in a marijuana leaf? And over 4,000 chemicals besides nicotine are in tobacco!

The brain is your body

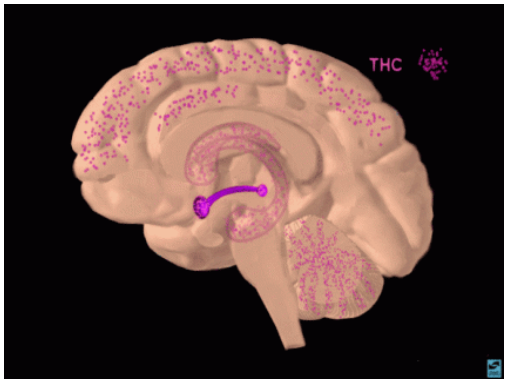


Your brain controls *more* than the way you think. The brain controls our physical sensations and body movements. How we understand what we see, hear, smell, taste, and touch. Our sense of balance and coordination. Memory. Feelings of pleasure and reward. The ability to make judgments. When we catch a football, dance, jog, speak, sing, laugh, whistle, smile, cry - that's our brain receiving, processing, and sending out messages to different parts of our body.

When we feel good for whatever reason - laughing with a friend or seeing a good movie or eating our favorite ice cream - the brain's *reward system* is activated. As we said before, the reward system is the part of the brain that makes you feel good. The reward system is a collection of neurons that release dopamine, a neurotransmitter. When dopamine is released by these neurons, a person feels pleasure.

Scientists have linked dopamine to most drugs of abuse - including cocaine, marijuana, heroin, alcohol, and nicotine. These drugs all activate the reward system and cause neurons to release large amounts of dopamine. Over time, drugs damage this part of the brain. As a result of this damage, things that used to make you feel good - like eating ice cream, skateboarding, or getting a hug - no longer feel as good.

Control centers in the brain are affected by drug use



Drugs of abuse disable or disrupt important brain functions. When someone smokes marijuana, for example, the chemical THC (delta-9-tetrahydrocannabinol), the main psychoactive ingredient in marijuana, travels quickly to the brain. We can see the areas of the brain (in dark pink) where THC concentrates. Let's go back to the previous image and see the areas of the brain that are affected by THC. You can see that THC builds up in areas that control the body's movements, balance, coordination, memory and judgment abilities, and sensations. THC disrupts your brain's ability to control these activities as well as you could normally.

A positron emission tomography (PET) scanner

Now let’s take a look inside your mind... One of the tools that scientists use to see the effects of drugs on the brain is called positron emission tomography or a PET **[say the word “pet”]** scan. Similar to an x-ray, but much more sophisticated, a PET scan is used to examine many different organs including the heart, liver, lungs, and bones, as well as the brain. A PET scan shows much more than the physical structure of bone and tissue. A PET scan shows how well (or how little) an organ is functioning.

Using a PET scan, a doctor or a scientist can see what is actually happening in a person’s brain and see the effects of drugs. The PET scan shows areas of the brain that are active and also areas that are inactive or not functioning at all. Typically, a PET scan takes 1 to 2 hours with the person lying completely still so that the PET images will be clear.

Let’s see the effects a drug like cocaine has on the brain.

This is literally the brain on drugs

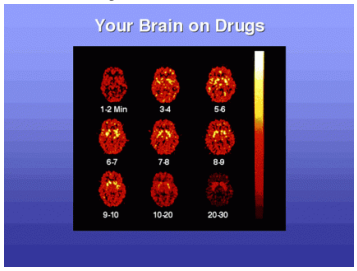


Photo courtesy of Nora Volkow, Ph.D. Mapping cocaine binding sites in human and baboon brain in vivo. Fowler JS, Volkow ND, Wolf AP, Dewey SL, Schlyer DJ, Macgregor, Hitzemann R, Logan J, Bendreim B, Gatley ST, et al. Synapse 1989;4(4):371-377.

When someone gets "high" on cocaine, where does the cocaine go in the brain? With the help of a radioactive tracer, this PET scan shows us a person's brain on cocaine and the area of the brain, highlighted in yellow, where cocaine is "binding" or attaching itself. This PET scan shows us minute by minute, in a time-lapsed sequence, just how quickly cocaine begins affecting a particular area of the brain

We start in the upper left hand corner. You can see that 1 minute after cocaine is administered to this subject nothing much happens. All areas of the brain are functioning normally. But after 3 to 4 minutes [the next scan to the right], we see some areas starting to turn yellow. These areas are part of a brain structure called the striatum [stry-a-tum] that is the main target in the brain bound and activated by cocaine.

At the 5- to 8-minute interval, we see that cocaine is affecting a large area of the brain. After that, the drug's effects begin to wear off. At the 9- to 10-minute point, the high feeling is almost gone. Unless the abuser takes *more* cocaine, the experience is over in about 20 to 30 minutes.

Scientists are doing research to find out if the striatum produces the "high feeling" and controls our feelings of pleasure and motivation. One of the reasons scientists are curious about specific areas of the brain affected by drugs such as cocaine is to develop treatments for people who become *addicted* to these drugs. Scientists hope to find the most effective way to change an addicted brain back to normal functioning.

Long-term effects of drug abuse

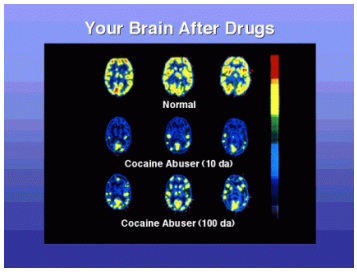


Photo courtesy of Nora Volkow, Ph.D. Volkow ND, Hitzemann R, Wang G-J, Fowler JS, Wolf AP, Dewey SL. Long-term frontal brain metabolic changes in cocaine abusers. Synapse 11:184-190, 1992; Volkow ND, Fowler JS, Wang G-J, Hitzemann R, Logan J, Schlyer D, Dewey S, Wolf AP. Decreased dopamine D2 receptor availability is associated with reduced frontal metabolism in cocaine abusers. Synapse 14:169-177, 1993.

This PET scan shows us that once addicted to a drug like cocaine, the brain is affected for a long, long time. In other words, once addicted, the brain is literally changed. Let's see how...

In this image, the level of brain function is indicated in yellow. The top row shows a normal-functioning brain without drugs. You can see a lot of brain activity. In other words, there is a lot of yellow color.

The middle row shows a cocaine addict's brain after 10 days without any cocaine use at all. What is happening here? **[Pause for response.]** *Less yellow* means *less normal activity* occurring in the brain - even after the cocaine abuser has abstained from the drug for 10 days.

The third row shows the same addict's brain after 100 days without any cocaine. We can see a little more yellow, so there is some improvement - more brain activity - at this point. But the addict's brain is *still* not back to a normal level of functioning... more than 3 months later. Scientists are concerned that there may be areas in the brain that never fully recover from drug abuse and addiction.

Drugs have long-term consequences

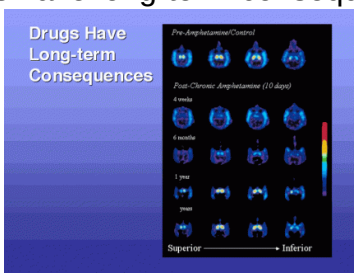


Photo courtesy of NIDA from research conducted by Melega WP, Raleigh MJ, Stout DB, Lacan C, Huang SC, Phelps ME. Recovery of striatal dopamine function after acute amphetamine- and methamphetamine-induced neurotoxicity in the vervet monkey. Brain Res 1997 Aug 22;766(1-2);113-120.

Here is another example of what science has shown us about the long-term effects of drugs. What this PET scan shows us is how just 10 days of drug use can produce very dramatic and long-term changes in the brain of a monkey. The drug in these images is amphetamine, or what some people call "speed." Remember the previous image showed us what the brain of a chronic cocaine abuser looks like. This image shows us what using a drug like amphetamine can do in only 10 days to the brain of a monkey.

This image also gives us a better idea of what methamphetamine, a drug similar in structure, can do to the brain. Methamphetamine use is becoming increasingly popular in certain areas of the country.

The top row shows us, in white and red, normal brain activity. The second row shows us that same brain 4 weeks *after* being given amphetamine for 10 days. There is a dramatic decrease in brain activity. This decreased brain activity continues for up to 1 year after amphetamine use. These continuous brain changes often trigger other changes in social and emotional behavior, too, including a possible increase in aggressiveness, feelings of isolation, and depression.

The memory of drugs

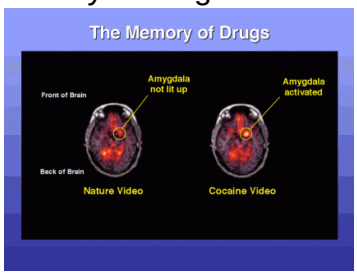


Photo courtesy of Anna Rose Childress, Ph.D.

This image demonstrates something really amazing - how just the *mention* of items associated with drug use may cause an addict to “crave” or desire drugs. This PET scan is part of a scientific study that compared recovering addicts, who had stopped using cocaine, with people who had no history of cocaine use. The study hoped to determine what parts of the brain are activated when drugs are craved.

For this study, brain scans were performed while subjects watched two videos. The first video, a nondrug presentation, showed nature images - mountains, rivers, animals, flowers, trees. The second video showed cocaine and drug paraphernalia, such as pipes, needles, matches, and other items familiar to addicts.

This is how the memory of drugs works: The yellow area on the upper part of the second image is the amygdala **(a-mig-duh-luh)**, a part of the brain’s limbic system, which is critical for memory

and responsible for evoking emotions. For an addict, when a drug craving occurs, the amygdala becomes active and a craving for cocaine is triggered.

So if it's the middle of the night, raining, snowing, it doesn't matter. This craving demands the drug *immediately*. Rational thoughts are dismissed by the uncontrollable desire for drugs. At this point, a basic change has occurred in the brain. The person is no longer in control. This *changed brain* makes it almost impossible for drug addicts to stay drug-free without professional help. Because *addiction* is a *brain disease*.

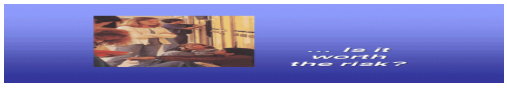
A message to remember

Courtesy of Partnership for a Drug Free America.

We discussed many important points today. Two points, in particular, I hope you remember. One is that drug abuse and addiction affect every segment of society. That's all of us. Everyone. Not one person is immune from the disease of addiction.

These images today demonstrate that there are observable changes in brain function that take place when drugs are used. We saw that the brains of addicts are different from the brains of people who are not addicted. And it is difficult, in some cases impossible, to return the brain to normal. Scientists, like those who work at the National Institute on Drug Abuse, are working to develop treatments to help people who are addicted to drugs. But treatment, like addiction, is a complex issue.

Is it worth the risk?



What percentage of people who experiment with drugs will become addicted? **[Pause for responses.]** Right now, science doesn't have the answer to that question. The effects of drugs on the brain are still being studied and explored.

And when we talk about drugs, we are not just talking about cocaine and marijuana and amphetamines and inhalants. Nicotine is highly addictive too, and, for many people, so is alcohol. Forget the stereotype of a drug addict hanging out on a dangerous street corner. Anyone can get hooked on drugs - your friends, members of your family, your neighbors.

Trying a drug just because a friend says it's "cool," might cost you much more than you bargained for. So every person in this room has to decide for themselves: Is it worth the risk?

The good news is: Help is available.

Visit NIDA

We've covered a lot of ground today. By now everyone here should have an idea of what drugs do to our brain, but the information we shared today is just a beginning. There's much more to discover about how the brain works. Take some time on your own to learn about this subject. The Internet is an excellent place to start.

To learn more, check out NIDA's home page on the World Wide Web and see what you can find out about the latest discoveries about the brain and how it responds to drugs.

For scientists, the brain is unexplored territory like the surface of Mars for the Pathfinder expedition. It is my hope that some of you will become scientists interested in how the brain

works, so that you might help us understand more about addiction and help us solve this problem.

Have you changed your mind?

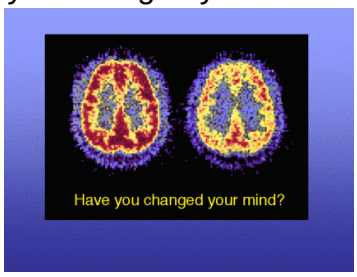


Photo courtesy of NIDA. If You Change Your Mind. Student magazine. NIH Publication No. 93-3474, 1993.

Here is our last image. As we look at side-by-side PET scans of a person who has never used cocaine compared with a cocaine addict, can you tell which brain is more active and healthy? Take a guess. Yes, the brain on the left with an abundance of *red* is the healthy, active brain.

With a little bit of knowledge about what drug addiction actually is, *anyone* - not just neuroscientists and neurobiologists - can see the changes in brain activity caused by drug abuse and addiction. The PET scans we've looked at today prove that.

We've seen the scientific facts. We've learned that addiction is a brain disease. And we've also learned that scientists are making great strides in developing treatments for addiction. There will be no magic charm to make addiction go away. But educated and informed with the scientific facts about what drugs can do to the brain, we are each in a better position to decide whether or not to take drugs in the first place. Given the facts, have *you* changed your mind?